

Hypovitaminosis D Among Healthy Children in the United States

A Review of the Current Evidence

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Objective: To review the published literature on serum 25-hydroxyvitamin D concentrations in US children.

Data Sources: Articles were identified by searching MEDLINE using *25-hydroxyvitamin D*, *vitamin D*, *hypovitaminosis D*, *vitamin D insufficiency*, *vitamin D deficiency*, *children*, and *adolescents* as key words and by screening references from original studies.

Study Selection: Studies were included if they fulfilled the following a priori criteria: contained a well-defined sample of children, included only healthy children, presented data on serum 25-hydroxyvitamin D concentrations, were published in the past 10 years, and were conducted in the United States.

Data Extraction: Serum 25-hydroxyvitamin D concentrations and prevalence of low vitamin D status (hypovitaminosis D).

Data Synthesis: Fourteen articles fulfilled the criteria. There were no consistent definitions of hypovitaminosis D; values corresponding to vitamin D defi-

ciency ranged from less than 5 ng/mL to less than 12 ng/mL, and those for vitamin D insufficiency ranged from less than 10 ng/mL to less than 32 ng/mL (to convert 25-hydroxyvitamin D concentrations to nanomoles per liter, multiply by 2.496). The following assays were used: radioimmunoassay (7 studies), competitive binding protein assay (3 studies), automated chemiluminescence protein-binding assay (3 studies), and enzyme-linked immunosorbent assay (1 study). Breastfed infants in winter who did not receive vitamin D supplementation were the most severely vitamin D deficient (78%). Estimates of the prevalence of hypovitaminosis D ranged from 1% to 78%. Older age, winter season, higher body mass index, black race/ethnicity, and elevated parathyroid hormone concentrations were associated with lower 25-hydroxyvitamin D concentrations.

Conclusion: Although overt vitamin D deficiency is no longer common in US children, lesser degrees of vitamin D insufficiency are widespread.

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IN THE 19TH CENTURY, AN EPIDEMIC of vitamin D-deficient rickets was present among US children.¹ The encouragement of sensible sunlight exposure and the fortification of milk with vitamin D resulted in an almost complete eradication of rickets by the mid 1900s.² Nevertheless, there have been recent reports of rickets in the United States; the affected have primarily been dark-skinned exclusively breastfed infants.^{3,4} Furthermore, while rickets is the extreme consequence of vitamin D deficiency, lesser degrees of vitamin D insufficiency may have important health consequences.⁵ Secondary hyperparathyroidism from vitamin D deficiency or insufficiency results in calcium being released from bone to maintain normal serum calcium levels.⁶ Because peak bone mass

achieved early in life is a predictor of the risk of osteoporosis in adulthood,⁷ it is important to optimize modifiable factors that affect bone mass acquisition in childhood, including vitamin D status. Moreover, findings from recent studies suggest that adequate levels of vitamin D may reduce the risk of type 1 diabetes mellitus,⁸ hypertension,⁹ and cancer.¹⁰ Therefore, it is now recognized that the health consequences of vitamin D status extend beyond the skeletal system.¹¹

The best indicator of vitamin D status is the serum 25-hydroxyvitamin D concentration because it is not regulated and reflects dietary intake from vitamin D₂ or vitamin D₃ and cutaneous synthesis of vitamin D₃.¹² No consensus on optimal concentrations of serum 25-hydroxyvitamin D exists; however, a cutoff of 10 ng/mL to

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Table 1. Lawful Addition of Vitamin D to Foods in the United States^a

Category of Food	Fortification Status	Maximum Level Allowed ^b	Surveyed Products Fortified With Vitamin D	
			Estimated No. Fortified	Usual Fortification Level
Cereal flours and related products				
Enriched farina	Optional	350 IU/100 g	Few	...
Ready-to-eat breakfast cereals	Optional	350 IU/100 g	Most	40-140 IU (10%-35% DV)
Enriched rice	Optional	90 IU/100 g	None	None
Enriched corn meal products	Optional	90 IU/100 g	None	None
Enriched noodle products	Optional	90 IU/100 g	None	None
Enriched macaroni products	Optional	90 IU/100 g	Very few	40 IU/252 g (10% DV)
Milk				
Fluid milk	Optional	42 IU/100 g	All	400 IU/quart
Acidified milk	Optional	42 IU/100 g	All	400 IU/quart
Cultured milk	Optional	42 IU/100 g	All	400 IU/quart
Concentrated milk	Optional	42 IU/100 g	All	400 IU/quart
Nonfat dry milk, fortified with A and D	Required	42 IU/100 g	All	400 IU/quart
Evaporated milk, fortified	Required	42 IU/100 g	All	400 IU/quart
Dry whole milk	Optional	42 IU/100 g	All	400 IU/quart
Milk products				
Yogurt	Optional	89 IU/100 g	Few	40-80 IU/RACC
Low-fat yogurt	Optional	89 IU/100 g	Few	40-80 IU/RACC
Nonfat yogurt	Optional	89 IU/100 g	Few	40-80 IU/RACC
Margarine	Optional	331 IU/100 g	Few	40-140 IU/RACC
Calcium-fortified fruit juices and drinks ^c	Optional	100 IU/RACC	Not appropriate ^d	100 IU/RACC

Abbreviations: DV, daily value; RACC, reference amount customarily consumed (or the US Food and Drug Administration's regulatory serving size); ellipses, not routinely fortified.

^aAdapted from Calvo et al¹⁸ with permission.

^bMaximum level of vitamin D that can be added in accord with 21 CFR §184.1(b)(2) for the category of food.

^cVitamin D₃ may be added at levels not to exceed 100 IU per serving to 100% fruit juices, excluding fruit juices that are specially formulated or processed for infants, which are fortified with more than 33% of the Dietary References Intake of calcium per serving.

^dIt is premature to evaluate the number of products in the marketplace given that the regulation was approved in April 2003.

15 ng/mL (to convert 25-hydroxyvitamin D concentrations to nanomoles per liter, multiply by 2.496) is typically used to define vitamin D deficiency. In its Dietary Reference Intakes, the Institute of Medicine¹² defines vitamin D deficiency as a 25-hydroxyvitamin D concentration less than 11 ng/mL, which may be too low because studies^{13,14} in adults have demonstrated that parathyroid hormone concentrations are at their ideal physiologic concentrations when 25-hydroxyvitamin D concentrations are above 32 ng/mL. Similar data in children are unavailable. The measurement of 1,25-dihydroxyvitamin D provides little additional insight into vitamin D status because of its tight physiologic control. Serum concentrations of 1,25-dihydroxyvitamin D are often normal in a vitamin D-deficient state because physiologic secondary hyperparathyroidism will increase renal production of 1,25-dihydroxyvitamin D.^{15,16} Additional information on the adequacy of vitamin D and calcium homeostasis can be obtained by measuring the parathyroid hormone concentration.

Dietary requirements for vitamin D were last set by the Institute of Medicine¹² in 1997. At that time, there was thought to be insufficient information to establish an Estimated Average Requirement, so an Adequate Intake was set.¹² The Adequate Intake for vitamin D among children is 200 IU.¹² Few foods naturally contain vitamin D. Although certain fatty fishes are thought to contain large amounts of naturally occurring vitamin D, the vitamin D content varies widely even within species.¹⁷ Various foods

are eligible for vitamin D fortification; however, there is a wide gap between the number of eligible foods and those actually fortified (**Table 1**).¹⁸ Fluid milk is the only dairy food routinely fortified with vitamin D, and its content varies significantly depending on factors that include storage conditions for the vitamin preparation, the method used to add vitamin D to the milk, and the point during processing at which it is added.¹⁸ Reports of underfortified milk have been published.¹⁹⁻²² Infant formulas also exhibit wide variability in vitamin D content.²³

Vitamin D is a unique nutrient because it can be synthesized endogenously. The skin is the major source of vitamin D production, and most persons meet their requirements by casual sunlight exposure.¹³ Factors affecting the ability to cutaneously synthesize vitamin D₃ include age, season, latitude, time of day, skin pigmentation, amount of skin exposed, and the use of sunscreen with a sun protective factor higher than 8.¹³ Exposure to sunlight for 5 to 15 minutes (between 10 AM and 3 PM) during the spring, summer, and fall provides lighter-skinned persons with adequate vitamin D.²⁴ Persons of black race/ethnicity require approximately 5 to 10 times longer exposure than persons of white race/ethnicity to produce vitamin D₃.²⁵ In addition, persons living above 35° latitude cannot produce adequate previtamin D₃ during winter.²⁶

To describe the current evidence of hypovitaminosis D in healthy US children, we systematically reviewed recent studies of 25-hydroxyvitamin D concentrations reported in children from birth through 18 years of age.

Table 2. Recent Studies of Vitamin D Status in US Children

Source	Method Used to Determine Serum 25-Hydroxyvitamin D Concentrations	Method Used to Determine Parathyroid Hormone Concentrations	Factors Associated With 25-Hydroxyvitamin D Concentrations
Weng et al, ²⁷ 2007	RIA	CLA	Older age, black race/ethnicity, winter study visit, total daily vitamin D intake <200 IU
Willis et al, ²⁸ 2007 ^a	RIA	Not measured	Race/ethnicity, season, age
Bodnar et al, ²⁹ 2007	ELISA	Not measured	Race/ethnicity, season
Kemp et al, ³⁰ 2007	RIA	Not measured	Race/ethnicity, season, age
Lee et al, ³¹ 2007	CBPA	Not measured	Correlation between infant and maternal 25-hydroxyvitamin D concentrations
Stein et al, ³² 2006 ^a	RIA	Not measured	Race/ethnicity, season
Ziegler et al, ³³ 2006	RIA	IRMA	Darker skin, winter season, no vitamin D supplementation
Harkness and Cromer, ³⁴ 2005 ^b	Automated CLBPA	Not measured	Race/ethnicity, season
Harkness and Cromer, ³⁵ 2005 ^b	Automated CLPBA	IRMA	Race/ethnicity, season, parathyroid hormone concentration
Sullivan et al, ³⁶ 2005	CBPA	CLA	Season
Rajakumar et al, ³⁷ 2005	Automated CLBPA	CLA	Tanner stage, calcium intake
Abrams et al, ³⁸ 2005	RIA	IRMA	Race/ethnicity, season, parathyroid hormone concentration
Gordon et al, ³⁹ 2004	CBPA	CLA	Season, race/ethnicity, milk and juice consumption, body mass index, physical activity
Looker et al, ⁴⁰ 2002	RIA	Not measured	Race/ethnicity, season

Abbreviations: CBPA, competitive binding protein assay; CLA, chemiluminescence assay; CLPBA, chemiluminescence protein-binding assay; ELISA, enzyme-linked immunosorbent assay; IRMA, immunoradiometric kit; RIA, radioimmunoassay.

^aThese studies contain data from the same subjects.

^bThese studies contain data from the same subjects.

We included only studies from the United States because food sources of vitamin D vary by country due to differences in the food supply and in fortification laws.

METHODS

INCLUSION CRITERIA

Studies were included in this review if they fulfilled the following a priori defined set of criteria: (1) contained a well-defined sample of children, (2) included only healthy children, (3) presented data on serum 25-hydroxyvitamin D concentrations, (4) were published in the past 10 years, and (5) were conducted in the United States. Articles that included only children with vitamin D-deficient rickets were excluded because the goal was to review vitamin D status in healthy children.

SEARCH OF STUDIES

Search strategies included (1) a computerized MEDLINE search for English-language studies that examined vitamin D status in children and (2) a screening of the reference lists from original studies. The following key words were used: 25-hydroxyvitamin D, vitamin D, hypovitaminosis D, vitamin D insufficiency, vitamin D deficiency, children, and adolescents.

RESULTS

LITERATURE SEARCH

Fourteen articles fulfilled all 5 inclusion criteria (**Table 2**).²⁷⁻⁴⁰ Two pairs of articles (studies by Willis

et al²⁸ and Stein et al³² and 2 studies by Harkness and Cromer^{34,35}) published data derived from the same samples. In 13 of the studies, the following 8 geographic locations were represented: Pennsylvania,^{27,29,37} Georgia,^{28,32} New Jersey,³⁰ Iowa,³³ Ohio,^{34,35} Texas,³⁸ Maine,³⁶ and Massachusetts.^{31,39} One study⁴⁰ consisted of a nationally representative sample of children.

SUMMARY OF FINDINGS

No consistent definitions of vitamin D deficiency or vitamin D insufficiency were used, and several studies used multiple cut points for low vitamin D status based on 25-hydroxyvitamin D concentrations. Some studies reported 25-hydroxyvitamin D concentrations in nanomoles per liter, while others reported results in nanograms per milliliter. The values corresponding to vitamin D deficiency ranged from less than 5 ng/mL to less than 12 ng/mL, and for vitamin D insufficiency they ranged from less than 10 ng/mL to less than 32 ng/mL. In addition, there was considerable variability in the assay used to measure 25-hydroxyvitamin D concentrations: 7 studies^{27,28,30,32,33,38,40} used a radioimmunoassay, 3 studies^{31,36,39} used a competitive binding protein assay, 3 studies^{34,35,37} used an automated chemiluminescence protein-binding assay, and 1 study²⁹ used an enzyme-linked immunosorbent assay. Because of other methodological differences (such as the ability of assays to detect both vitamin D₂ and D₃), there is often substantial variability among results from different assays.⁴¹⁻⁴⁴ The method most commonly used in the studies reviewed, radioim-

immunoassay, compares well with the gold standard high-performance liquid chromatography method.⁴⁵ Only 7 of 14 studies also measured intact parathyroid hormone concentrations: 3 studies^{33,34,38} used an immunoradiometric kit, and 4 studies^{27,36,37,39} used a chemiluminescence assay.

The studies are reviewed according to the life stages: neonates, infants, and children (>1 year). These groups were chosen because (1) neonates are completely dependent on their mother's vitamin D stores, (2) infants likely consume some food sources of vitamin D and may be exposed to some sunlight, and (3) children most likely consume food sources of vitamin D and are exposed to more sunlight.

Neonates

Two studies^{29,31} examined the vitamin D status of neonates by measuring 25-hydroxyvitamin D concentrations in cord blood or serum shortly after birth. Neither study measured parathyroid hormone concentrations. One study³¹ consisted of 40 mother-newborn pairs (25 black, 10 white, 3 Asian, and 2 biracial) from Boston Medical Center, Boston, Massachusetts (latitude, 42° north), in which blood samples were obtained from neonates born between October and February at 24 to 48 hours after birth. Sixty-five percent (n=26) were vitamin D deficient (<12 ng/mL), and neonate and maternal 25-hydroxyvitamin D concentrations were positively correlated (r=0.68). A larger study²⁹ examined 25-hydroxyvitamin D concentrations in cord blood of 400 neonates (200 black and 200 white) in Pittsburgh, Pennsylvania (latitude, 40° north). Neonates were classified as vitamin D deficient (<15 ng/mL), vitamin D insufficient (15-32 ng/mL), or vitamin D sufficient (>32 ng/mL). Among white neonates, 9.7% had vitamin D deficiency, and 56.4% had vitamin D insufficiency. White neonates born in the spring had a 76% increased prevalence of vitamin D insufficiency compared with white neonates born in the summer. Among black neonates, 45.6% were vitamin D deficient, and 46.8% were vitamin D insufficient. There were no seasonal effects of vitamin D status in black neonates, which is likely caused by their low vitamin D status throughout the year. Cord blood 25-hydroxyvitamin D concentrations were strongly correlated with maternal serum levels before delivery (r=0.89).

Infants

One study³³ among healthy infants was published in the past 10 years (although several other investigations were identified, they included only infants with rickets). Eighty-four breastfed infants (77 white, 3 black, 3 Asian, and 1 Pacific Islander) from Iowa (latitude, 41° north) were examined at age 280 days. Ten percent of the infants (n=8) were vitamin D deficient (<11 ng/mL). Fifty-eight percent (n=49) of the infants received vitamin D from formula (n=45), vitamin supplements (n=3), or both (n=1). Infants were enrolled in this study before the publication of the American Association of Pediatrics⁴⁶ guidelines on vitamin D supplementation. Vitamin D deficiency was more prevalent among infants who did not receive supplementation with vitamin D, and the sea-

sonal effects were more pronounced among infants who did not receive supplementation (78% were deficient in winter vs 4% in summer). No infants who received supplementation were vitamin D deficient. The mean (SD) intact parathyroid hormone concentration was higher in vitamin D-deficient infants (32.9 [16.2] pg/mL) compared with vitamin D-sufficient infants (16.0 [12.9] pg/mL) (to convert parathyroid hormone concentrations to nanograms per liter, multiply by 1.0). At 112 days of life, 70% of the infants who did not receive supplementation were vitamin D deficient.

Children Older Than 1 Year

Eleven studies (detailed herein) examined vitamin D concentrations in subjects aged 1 to 21 years. Because of the variability among age ranges in each study, it was impossible to further divide this category into smaller age groupings.

The most recent study²⁷ examined 382 healthy children (age range, 6-21 years) from the Philadelphia, Pennsylvania, area (latitude, 40° north). Among children examined during winter, the overall prevalence of hypovitaminosis D (<30 ng/mL) was 68% (51% among whites and 94% among blacks). Low vitamin D status was more likely to occur in subjects who had greater fat mass and higher body mass index z scores, in subjects who were evaluated during winter months, and in subjects who were older, black, members of households with lower annual incomes, and members of households with lower caregiver education levels. In addition, low vitamin D status was associated with lower dietary, supplemental, and total daily intake of vitamin D. Parathyroid hormone concentrations were inversely associated with 25-hydroxyvitamin D concentrations (r=-0.31).

Two studies^{28,32} conducted in Athens, Georgia (latitude, 34° north), examined black and white girls (age range, 4-8 years) enrolled in a prospective study of the effect of gymnastic training on bone mineral accrual. The initial study³² reported cross-sectional results from 168 girls at baseline. None had 25-hydroxyvitamin D concentrations less than 11 ng/mL, and less than 1% of the sample (n=5) had 25-hydroxyvitamin D concentrations less than 20 ng/mL. Season and race/ethnicity were predictors of vitamin D status. In the follow-up study,²⁸ 25-hydroxyvitamin D concentrations were reported longitudinally among the girls in the nonintervention group. Eighteen percent had 25-hydroxyvitamin D concentrations less than 20 ng/mL, with 75% having levels less than 32 ng/mL (at ≥1 time point during the follow-up period). Age, season, and race/ethnicity remained significant predictors of 25-hydroxyvitamin D concentrations after adjusting for calcium intake, vitamin D intake, and physical activity. However, after adjusting for fat-free mass, only season and race/ethnicity remained significant. Neither study measured parathyroid hormone concentrations.

A study³⁰ of 142 black and Hispanic children (age range, 1-8 years) from a women, infants, and children's clinic in Newark, New Jersey (latitude, 40° north), examined paired winter and summer 25-hydroxyvitamin D concentrations. Twelve percent of children had low 25-hydroxyvitamin D concentrations in winter, and 0.7% had

low 25-hydroxyvitamin D concentrations in summer. Vitamin D deficiency was most frequent in black children aged 4 to 8 years during winter. This study did not measure parathyroid hormone concentrations.

Two articles were published from the same cohort of postmenarchal girls (age range, 12-18 years) in the greater Cleveland, Ohio, area (latitude, 41° north).^{34,35} Participants were eligible for a clinical trial on contraceptives; however, no further details were provided. Girls were classified as black (n=254) or as nonblack (n=146). The non-black group included 131 white non-Hispanics, 12 white Hispanics, 2 Asians, and 1 Native American. The first study³⁵ from this cohort reported that 17% of the girls were vitamin D deficient (≤ 11 ng/mL) and 54% were vitamin D insufficient (< 20 ng/mL). These rates differed by ethnic group; 26% of blacks and 1% of nonblacks were vitamin D deficient. There were also significant seasonal variations in 25-hydroxyvitamin D concentrations between racial/ethnic groups. The second study³⁴ from this cohort of girls examined the relationship between 25-hydroxyvitamin D concentrations and parathyroid hormone concentrations. There was a significant negative correlation between 25-hydroxyvitamin D concentrations and parathyroid hormone concentrations ($r = -0.314$). An increase in parathyroid hormone concentrations was observed when 25-hydroxyvitamin D concentrations decreased below 36 ng/mL. There was a stronger correlation between 25-hydroxyvitamin D concentrations and parathyroid hormone concentrations in nonblack girls ($r = -0.28$) than in black girls ($r = -0.19$).

An observational study³⁶ of bone mineralization in 23 white adolescent girls (age range, 9-11 years) in the Bangor, Maine, area (latitude, 44° north) was conducted. For 3 consecutive years, 25-hydroxyvitamin D concentrations and parathyroid hormone concentrations were measured every September and every March. Forty-eight percent (n=11) were vitamin D deficient (< 20 ng/mL) at some point during the 3 years, and 17% (n=4) exhibited vitamin D deficiency in September and in March. There was a consistent decrease in 25-hydroxyvitamin D concentrations between September and March across years, with a mean decrease of 8 ng/mL. The mean increase in intact parathyroid hormone between September and March was 4.0 pg/mL.

Another study³⁷ examined 41 black children (age range, 6-10 years) from the Pittsburgh area (latitude, 40° north). Children were recruited during winter and early spring, and 49% (n=20) had vitamin D insufficiency (≤ 20 ng/mL). These children then received vitamin D supplementation with 400 IU/d for 1 month, and 18% remained vitamin D insufficient, which was likely due to the short duration of treatment or an inadequate vitamin D dosage.

A multiethnic sample of 93 children (age range, 10-14 years) from the Houston, Texas, area (latitude, 30° north) participated in a calcium absorption study.³⁸ One child (1%) had a 25-hydroxyvitamin D concentration less than 12 ng/mL, 15 children (16%) had levels less than 20 ng/mL, and 68 children (73%) had levels less than 32 ng/mL. Eighteen children (19%) had parathyroid hormone concentrations greater than 50 pg/mL, and 5 children (5%) had levels greater than 80 pg/mL. Season, race/ethnicity, and

parathyroid hormone concentrations were significant predictors of 25-hydroxyvitamin D concentrations. Season and parathyroid hormone concentrations were related to calcium absorption, but 25-hydroxyvitamin D concentrations were not.

Three hundred seven primary care patients (age range, 11-18 years) from Children's Hospital in Boston (latitude, 42° north) were enrolled in an observational study³⁹ during annual physical examinations. Twenty-four percent (n=74) were vitamin D deficient (≤ 15 ng/mL), of whom 5% (n=14) were severely vitamin D deficient (≤ 8 ng/mL). In addition, 42% (n=129) were vitamin D insufficient (< 20 ng/mL). There was a significant correlation between 25-hydroxyvitamin D concentrations and parathyroid hormone concentrations ($r = -0.29$). In a multivariate model, season, race/ethnicity, physical activity, body mass index, and milk and juice consumption were significant predictors of hypovitaminosis D.

The only nationally representative study⁴⁰ was from the Third National Health and Nutrition Examination Survey. Data were collected in northern latitudes (range, 25°-47° north) during summer and in southern latitudes during winter because assessments were performed in a mobile van. To address seasonality, the sample was stratified into 2 groups based on the month of blood sample collection, November to March or April to October. During winter, vitamin D insufficiency (< 25 ng/mL) was observed in 25% of male subjects and in 47% of female subjects aged 12 to 19 years in the lower latitudes. During summer, 21% of male subjects and 28% of female subjects in the higher latitudes were vitamin D insufficient. The prevalence of vitamin D deficiency was 1% or less among all groups except for female subjects in the group studied during winter in the lower latitudes, among whom the prevalence was 4%.

COMMENT

Hypovitaminosis D is common in healthy children throughout the United States. Factors consistently associated with 25-hydroxyvitamin D concentrations include age, season, and race/ethnicity. Additional factors frequently associated with vitamin D concentrations were vitamin D supplementation and parathyroid hormone concentrations; however, these were not examined in all studies. Comparing results among the 14 studies was challenging because there were no consistent definitions of vitamin D deficiency and vitamin D insufficiency, so prevalence estimates could not be determined. Despite this limitation, findings from the recent literature in aggregate strongly suggest that hypovitaminosis D affects healthy children of all ages and all races/ethnicities, not just dark-skinned infants whose diets are not adequately supplemented, the group that has received most of the attention.^{3,4,47,48} The full clinical effect of vitamin D insufficiency is still being elucidated, but it is reasonable to infer that low vitamin D status in children is undesirable not only for bone health but also for prevention of several chronic diseases later in life.

Future research efforts should focus on determining the optimal 25-hydroxyvitamin D concentrations for chil-

dren and on establishing the health consequences of hypovitaminosis D. In adults, this was done by examining investigations that evaluated thresholds for serum 25-hydroxyvitamin D concentrations in relation to outcomes, including bone mineral density, lower extremity function, and risk of falls, fractures, and colorectal cancer.⁵ Because many of these outcomes are irrelevant to children, other outcomes should be considered such as optimal calcium absorption and suppression of parathyroid hormone concentration to its ideal physiologic range. Fractures and bone mineral content can also be examined; however, these associations are harder to identify because acute measures of 25-hydroxyvitamin D concentrations may not reflect the mean levels achieved across a period of bone mineral acquisition. Once optimal 25-hydroxyvitamin D concentrations for children are established, the dosages of vitamin D required to achieve those levels should be determined.

As evidenced by the various methods used in the reviewed studies, there is a need for standardization of vitamin D assays. Variability exists among the methods, and a recent study⁴² reported discordant results from different laboratories that used different methods. In the study, 90% of women were considered vitamin D insufficient according to results from one laboratory, but only 17% were vitamin D insufficient when their serum samples were analyzed at another laboratory. The 2 major diagnostic laboratories now use liquid chromatography-tandem mass spectrometry to measure the 2 circulating forms of 25-hydroxyvitamin D; however, it is unlikely that all researchers will send their samples to an outside laboratory for analysis. Therefore, to potentially correct hypovitaminosis D in children and to investigate its clinical significance, standardization of definitions and 25-hydroxyvitamin D measurements is needed.

Public health efforts aimed at improving the vitamin D status of children are advisable, and several different approaches exist. Food fortification with vitamin D is one option because various foods in the United States are eligible for vitamin D fortification, but not all are routinely fortified.¹⁸ In recent years, there has been an increase in the number of vitamin D-fortified foods, including some orange juices and yogurts, but there are still more eligible foods that can be fortified.¹⁸ Since the 1997 Adequate Intakes for vitamin D were released,¹² new information has become available suggesting that the current Dietary Reference Intakes for vitamin D are too low to maintain adequate vitamin D concentrations in most children, and there is a movement in place to update these recommendations.⁴⁹ Another possibility is to educate the public about sensible sunlight exposure and to emphasize the minimal amount of time required to synthesize vitamin D. However, the risk of miscommunicating this limited time required for adequate vitamin D synthesis may belie the strong resistance from the American Academy of Dermatology to recommend sunlight exposure for maintaining adequate vitamin D concentrations. The American Academy of Dermatology⁵⁰ recommends getting vitamin D solely through diet. Similarly, the Centers for Disease Control and Prevention, with the support of other organizations, has launched a major public health campaign to decrease the incidence of skin can-

cer by urging people to limit exposure to UV light.⁵¹ These initiatives to decrease sunlight exposure in healthy people, including children, only increases the importance of determining effective dietary means of achieving optimal vitamin D concentrations.

In summary, although overt vitamin D deficiency is no longer common, lesser degrees of vitamin D insufficiency are widespread in children. It has become increasingly evident that vitamin D has several important functions in addition to its classic role in maintaining serum levels of calcium and phosphorus. Therefore, efforts are needed to improve the vitamin D status of children in the United States, and research is needed to determine how to most effectively achieve this goal.

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