Vitamin D requirements in adolescents: what is the target?¹⁻⁴

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For many decades, the vitamin D requirements for almost all pediatric populations were clear: either spend some time in the sun or obtain 400 IU daily from diet or a supplement. These guidelines took varying forms across the world but were based on the early observation that 400 IU vitamin D daily, the approximate amount in a teaspoon of cod liver oil, reliably prevented rickets in almost any child (1).

Since then, we have reconsidered the definition of dietary requirements and have added new terms to our nutrition policy statements. Depending on the definition, it is readily possible to find sources in the popular and medical literature advocating that children need as little as 10 min/d in the sun and no supplemental vitamin D to several thousand units of supplemental vitamin D daily. Almost every source claims authority and expertise, which leads to confusion and sharp disagreement about what really is required for health.

Into this mix have recently come several new guidelines from organizations or committees that can help families, dietitians, physicians, and others try to sort this issue out. In 2008, after careful review of the evidence, separate statements from the Pediatric Endocrine Society and from the American Academy of Pediatrics (AAP) Committee on Nutrition and Section on Breastfeeding each recommended 400 IU vitamin D daily, from diet or supplements, for most children and adolescents (2, 3). The Pediatric Endocrine Society statement indicated that consideration should be given to supplementing some groups of children with up to 800 IU vitamin D/d. On 30 November 2010, the Food and Nutrition Board of the Institute of Medicine (IOM) recommended 400 IU daily to meet the needs of half of children aged 1–18 y and 600 IU daily to meet the needs of 97.5% of these children (4). These new values (400 IU and 600 IU daily) define the Estimated Average Requirement and the Recommended Dietary Allowance (RDA), respectively. These are substantial increases from the 1997 Adequate Intake recommendations from the IOM of 200 IU/d for all children and adolescents (5).

In this issue of the Journal, Cashman et al (6) report on their evaluation of data from studies in white Danish and Finnish girls to determine the vitamin D intake that would achieve targeted 25-hydroxyvitamin D [25(OH)D] concentrations in the absence of a substantial amount of sunshine exposure. They found that an intake of 18.6 µg (~750 IU) daily would allow 97.5% of young adolescent girls to achieve a 25(OH)D concentration of ≥50 nmol/L. This is the lower end of the 25(OH)D range recommended by the Pediatric Endocrine Society as being adequate in children. It is the 25(OH)D concentration used for the RDA and considered by the IOM to meet the needs of nearly all children and adolescents (2–4).

Although slightly higher than the IOM value, the difference between the IOM vitamin D intake of 600 IU and the corresponding value of 750 IU derived by Cashman et al (6) that is required to reach 50 nmol/L in 97.5% of the population of female adolescents is relatively small. It is expected that data will be gathered in different populations as part of the ongoing process of refining pediatric-specific values for Dietary Reference Intakes that will have wide generalizability. As such, these data are important in continuing to develop more accurate and precise nutrient requirements in adolescents.

Taken together, these data indicate fairly clearly that intakes of ~400–800 IU/d will lead to achieved 25(OH)D concentrations ≥50 nmol/L in the vast majority of children and concentrations ≥30 nmol/L, which is the level required to prevent rickets, in essentially all children. Nonetheless, variability around these values is considerable, with higher values achieved where there is some sunshine exposure and in nonobese, lighter-skin individuals. Additional effects of disease processes, as well as genetic effects such as those related to vitamin D receptor polymorphisms, require further research.

In considering these data, it is worth reconsidering the “target.” What are the consequences for failure to achieve any given 25(OH)D value in adolescents? Here we enter more tentative territory. A series of pediatric studies have shown that above a 25(OH)D concentration of ~30 nmol/L there is minimal, if any, positive effect of higher 25(OH)D on calcium absorption (2, 7, 8). Whereas some studies have shown an effect on bone density, these effects are small and provide limited bone-related evidence for achieving concentrations of 25(OH)D in children and adolescents substantially above 40–50 nmol/L. Likewise,

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the proposed endpoint of minimizing parathyroid hormone concentrations by achieving higher 25(OH)D concentrations has not been able to identify a specific 25(OH)D target value (4). In adults, the targeted 25(OH)D concentration needed to maximize calcium absorption is similarly uncertain, leading to doubts about the biological meaning of 25(OH)D concentrations for calcium absorption outside of a negative effect of very low values (eg, <30 nmol/L) (9).

With regard to nonbone outcomes, the evidence in pediatric populations for a target intake of vitamin D or concentration of serum 25(OH)D is extremely limited. Most estimates are based on associations derived from observational studies with concerns about unidentified or inadequately considered covariates. In any case, drawing cause-and-effect conclusions from observational data should be done cautiously. One controlled trial, by Urashima et al (10), recently found a marginally significant \( P = 0.04 \) decrease in influenza A with vitamin D supplementation in Japanese children. However, claims that such a study is definitive or that vitamin D should be used in place of immunizations are poorly founded on the basis of current evidence. The study by Urashima et al had substantial limitations, including the finding that benefits were seen only in some subgroups, such as in those who started nursery school after age 3 y (10). There were 13 fewer cases of influenza A and 11 more cases of influenza B in the treatment group, so in fact no overall effect on total influenza cases was identified. The study also had a substantial dropout rate and was limited by a small sample size. Moreover, serum 25(OH)D was not measured in the study subjects. Much larger studies in multiple sites with few dropouts and more outcome measurements would be needed before dietary recommendations for the United States and Canada could be made on the basis of prevention or treatment of respiratory infections in children. Similarly, other nonbone outcomes in children and adolescents are in need of controlled trials in which efficacy and safety are evaluated in adequately sized groups of children.

What then should be done on the basis of the data and recommendations we currently have available? First, although sunshine is part of the vitamin D equation in most populations, it cannot be considered a reliable source in many pediatric populations and should not be relied on as the sole means of preventing vitamin D deficiency. Pediatric populations should have dietary vitamin D sources, supplemental vitamin D sources, or both as recommended by the AAP and the IOM (2, 5).

Second, it is reasonable to use the IOM RDA of 600 IU/d or the slightly higher value of 750 IU/d provided by Cashman et al (6) as a vitamin D intake goal in most individual adolescents, with the appreciation that further understanding and refinement of RDA values is an ongoing process. However, caution should be used before using a single study or small studies in select populations to adjust recommendations. Increased dietary vitamin D intake and the use of small supplements to reach daily vitamin D intakes of 600–750 IU are reasonable and practical options.

What comes next for scientists and clinicians? Two key topics not fully addressed by the IOM or the AAP and Pediatric Endocrine Society in their statements are determining the public policy implications of screening 25(OH)D concentrations in healthy children and determining what the potential benefits of vitamin D intakes well above the current RDA (eg, intakes of 2000–4000 IU/d) are on a range of health outcomes. In the former case, more data are needed to determine the potential individual and societal benefits, costs, and risks of routine measurement of serum 25(OH)D in healthy children before this becomes a care standard. Until then, screening decisions are best left to individual care providers on the basis of individualized, subject-specific factors, including a full medical history. When screened, differences in recommendations for the target 25(OH)D will need to be considered in making recommendations.

With regard to high-dose supplementation, it is critical that such studies be done for a range of pediatric health care outcomes. Ongoing studies of the effects of vitamin D related to cancer in adults will be important, but we need pediatric studies for a range of outcomes, especially those related to respiratory and neurologic illnesses. It is not appropriate to rely on data from adults to make decisions about children and adolescents regarding vitamin D. Many acute and chronic illnesses may be affected by vitamin D, and at this time epidemiologic studies need to be followed by controlled trials to answer cause-and-effect questions about possible benefits of vitamin D in prevention or treatment of these conditions. The new Tolerable Upper Intake Level of 4000 IU vitamin D/d (2500 IU/d for children aged 1–3 y and 3000 IU for children aged 4–8 y) (4) would be reasonable as an upper dose in many such studies, although with appropriate monitoring higher doses could be considered. Such studies are the only way we can answer the question related to vitamin D and non-bone-related outcomes in children.

For now, controversy about vitamin D requirements will persist. New statements and new research, such as the current Cashman et al (6) study, provide evidence-based information specific to pediatric populations. Much more such data are needed to allow us to move forward.

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REFERENCES