Guideline Update: Evaluation, Treatment, and Prevention of Vitamin D Deficiency

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Michael F. Holick, PhD, MD, Boston University School of Medicine, Boston, Massachusetts, USA, released findings from an Endocrine Society Task Force on updated guidelines for the evaluation, treatment, and prevention of vitamin D deficiency. Few foods naturally contain vitamins D_2 or D_3, and deficiency is common throughout the world across all age groups [Holick MF et al. *J Clin Endrinol Metab* 2011].

The updated clinical practice guidelines are based on a systematic review of the literature and represent the latest evidence-based findings [Holick MF et al. *J Clin Endrinol Metab* 2011].

Diagnostic Procedure

The Task Force recommends screening for vitamin D deficiency using the serum circulating 25-hydroxyvitamin D [25(OH)D] level, measured by a reliable assay in individuals who are at risk for vitamin D deficiency. Population screening for individuals who are not at risk is not recommended. Vitamin D deficiency is defined as a 25(OH)D level below 20 ng/ml (50 nmol/L). Vitamin D insufficiency is defined as a 25(OH)D level of 21–25 ng/ml (>5 nmol/L). The Task Force recommended against using the serum $1,25(OH)_2D$ assay to screen for deficiency. Rather, it should only be used to monitor certain conditions, such as acquired and inherited vitamin D and phosphate metabolism disorders.

Recommended Dietary Intakes for Patients at Risk for Vitamin D Deficiency

Infants and Children

Infants and children aged 0 to 1 year require at least 400 IU/day (IU=25 ng/ml) of vitamin D; those aged 1 year and older require at least 600 IU/day to maximize bone health. It remains unknown whether these doses are enough to optimize all potential nonskeletal health benefits that are associated with vitamin D. The ability to consistently raise the blood level of 25(OH)D above 30 ng/ml (75 nmol/L) may require at least 1000 IU/day of vitamin D.

- Adults Aged 19 to 50 Years

  Adults aged 19 to 50 years require at least 600 IU/day of vitamin D to maximize bone health and muscle function; however, at least 1500 to 2000 IU/day of vitamin D may be required to consistently raise the blood level of 25(OH)D above 30 ng/ml

- Adults Aged 50 to 70 Years

  All adults aged 50 to 70 years and 70+ years require at least 600 IU/day and 800 IU/day, respectively, of vitamin D to maximize bone health and muscle function; however, to consistently raise the blood level of 25(OH)D above 30 ng/ml may require at least 1500–2000 IU/day of supplemental vitamin D

- Pregnant and Lactating Women

  Pregnant and lactating women require at least 600 IU/d of vitamin D; however, at least 1500–2000 IU/day of vitamin D may be needed to maintain a blood level of 25(OH)D above 30 ng/ml

Peer-Reviewed Highlights from the

- Obesity, Anticonvulsants, Glucocorticoids, Antifungals, & AIDS Medications

  Obese children and adults, and patients who are taking anticonvulsant medications, glucocorticoids, antifungals (such as ketoconazole), and medications for AIDS should take at least 2 to 3 times more vitamin D than others in their age group to satisfy their bodies' vitamin D requirements.

Maintenance Tolerable Upper Limits

Maintenance tolerable upper limits (UL) of vitamin D are not to be exceeded without medical supervision. These should be 1000 IU/day for infants aged up to 6 months; 1500 IU/day for infants aged from 6 months to 1 year; at least 2500 IU/day for children aged 1 to 3 years; 3000 IU/day for children aged 4 to 8 years; and 4000 IU/day for everyone aged >8 years. Higher levels of 2000 IU/day for children aged 0 to 1 year, 4000 IU/day for children aged 1 to 18 years, and 10,000 IU/day for children and adults aged ≥19 years might be needed to correct vitamin D deficiency.

Treatment and Prevention Strategies for Those Who Are Vitamin D-Deficient

Either vitamin D_2 or vitamin D_3 should be used for the treatment and prevention of vitamin D deficiency.

- **Infants and toddlers (0 to 1 year)** who are vitamin D-deficient should be treated with 2000 IU/day of vitamin D_2 or vitamin D_3 or with 50,000 IU of vitamin D_2 or vitamin D_3 once weekly for 6 weeks to achieve a blood level of 25(OH)D above 30 ng/ml; maintenance therapy should be 400–1000 IU/day
- **Children aged 1 to 18 years** who are vitamin D-deficient should be treated with 2000 IU/day of vitamin D_2 or vitamin D_3 for at least 6 weeks or with 50,000 IU of vitamin D_2 once a week for at least 6 weeks to achieve a blood level of 25(OH)D above 30 ng/ml, followed by maintenance therapy of 600 to 1000 IU/day
- **All adults** who are vitamin D-deficient should be treated with 50,000 IU of vitamin D_2 or vitamin D_3 once a week for 8 weeks or the equivalent of 6000 IU of vitamin D_2 or vitamin D_3 daily to achieve a blood level of 25(OH)D above 30 ng/ml, followed by maintenance therapy of 1500–2000 IU/day
- **Patients who are obese, have malabsorption syndromes, and those on medications affecting vitamin D metabolism** should receive a higher dose (2 to 3 times higher; ie, at least 6000 to 10,000 IU/day) of vitamin D_2 or vitamin D_3 to treat deficiency and maintain a 25(OH)D level above 30 ng/ml; maintenance therapy should be 3000 to 6000 IU/day
- **Patients with extrarenal production of 1,25(OH)2D** should receive serial monitoring of 25(OH)D levels and serum calcium levels during treatment with vitamin D to prevent hypercalcemia
- **Patients with primary hyperparathyroidism** and vitamin D deficiency should receive treatment with vitamin D as needed; serum calcium levels should be monitored

Noncalcemic Benefits of Vitamin D

The Task Force recommended prescribing vitamin D supplementation for fall prevention. It did not recommend vitamin D supplementation beyond recommended daily needs for the purpose of preventing cardiovascular disease or death or improving quality-of-life (Table 1).

Table 1. Indications for 25(OH)D Measurement (Candidates for Screening).

- Rickets
- Osteomalacia
- Osteoporosis
- Chronic kidney disease
- Hepatic failure
- Malabsorption syndromes
  - Cystic fibrosis
  - Inflammatory bowel disease
- Crohn disease
- Bariatric surgery
- Radiation enteritis
- Hyperparathyroidism
- African-American and Hispanic children and adults
- Pregnant and lactating women
- Older adults with history of falls
- Medications
  - Antiseizure medications
  - Glucocorticoids
  - AIDS medications
  - Antifungals, *eg*, ketoconazole
  - Cholestyramine
- Older adults with history of nontraumatic fractures
- Obese children and adults (BMI≥30 kg/m^2)
- Granuloma-forming disorders
  - Sarcoidosis
  - Tuberculosis
  - Histoplasmosis
  - Coccidiomycosis
  - Berylliosis
- Some lymphomas

The major source of vitamin D for adults and children is unprotected sun exposure; without it, it is difficult, if not impossible, to obtain an adequate amount of vitamin D from dietary sources without supplementation. Concerns about melanoma and other types of skin cancer make it necessary to avoid excessive exposure to midday sun. Such worries strengthen the case for supplementation, especially among those who live at about 33º latitude [Grant WB et al. *Prog Biophys Mol Biol* 2009].