

Vitamin D Provides a Wide Range of Health Benefits: Implications for Cancer Prevention and the Treatment of Inflammatory and Metabolic Diseases and the Importance of Attaining Optimal Serum Levels of 25(OH)D

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An increasingly well-documented and consistent body of literature shows that vitamin D has clinically-significant anticancer and anti-inflammatory benefits, and that the attainment of optimal serum levels of vitamin D also confer protection against diabetes mellitus, insulin resistance, and hypertension. In this brief review, we will also discuss clinical trials that have used vitamin D in the treatment of polycystic ovary syndrome, migraine headaches, depression, epilepsy, and musculoskeletal pain. We also elucidate new guidelines for the interpretation of serum 25(OH)vitamin D levels.

Vitamin D deficiency is an underappreciated epidemic that has heretofore received insufficient attention from clinicians in all disciplines. Given the clinical consequences of hypovitaminosis D, it is indefensible that doctors fail to diagnose and treat this condition (ICD-9 code 268.x) since numerous studies have documented the remarkably high prevalence of vitamin D deficiency in medical patients (Kauppinen-Makelin R, et al. *J Intern Med.* 2001 Jun;249(6):559-63 and Thomas MK, et al. *N Engl J Med.* 1998 Mar 19;338(12):777-83). This article will serve to update clinicians on the diagnosis and treatment of this important and common health problem, and we have included our recommendations for laboratory testing to facilitate the clinical applicability of this information.

Vitamin D is metabolized in two distinct pathways: 1) endocrine—relevant to calcium absorption and bone metabolism, and 2) autocrine—relevant to the modulation of intracellular processes such as differentiation, proliferation, inflammation, and gene transcription. Relatedly, vitamin D deficiency is seen in two distinct forms: 1) acute deficiency diseases such as rickets and hypocalcemia, and 2) long-latency deficiency diseases which manifest only after years of subacute deficiency (Heaney RP. *Am J Clin Nutr.* 2003 Nov;78(5):912-9). According to the current research literature, long-term vitamin D deficiency contributes to an increased risk for cancer, type 1 diabetes, multiple sclerosis, hypertension, and insulin resistance, and each of these clinical entities will be discussed in the sections that follow.

- **Cancer:** Cancer risk and vitamin D deficiency go hand-in-hand. The risk of cancer in humans increases in direct proportion to the reduction in sun exposure, a fact that has been repeatedly verified since its first publication more than 60 years ago. Based on this extensive data, Dr William Grant has estimated that at least 23,000 and perhaps as many as 47,000 cancer deaths might be prevented each year in America if we employed simple interventions to raise vitamin D levels (*Cancer* 2002;94:1867-75).
- **Hypertension:** Suboptimal levels of vitamin D increase the risk for and severity of hypertension, and augmentation of vitamin D levels with sunlight or oral supplementation safely and consistently reduces blood pressure in hypertensive patients (Pfeifer M, et al. *J Clin Endocrinol Metab* 2001 Apr;86:1633-7)
- **Insulin resistance:** Patients with vitamin D deficiency show an increased prevalence of insulin resistance. Authors of a recent study concluded that improving vitamin D status such as with oral supplementation could improve insulin sensitivity by 60%, indicating that vitamin D treatment “is more potent than either troglitazone or metformin treatment (54% and 13% improvement in insulin sensitivity, respectively.)” (Chiu KC, et al. *Am J Clin Nutr* 2004; 79:820-5).
- **Depression:** Vitamin D administration was shown to improve mood within 5 days of treatment in a controlled clinical trial of patients with wintertime depression (Lansdowne AT, Provost SC. *Psychopharmacology* (Berl). 1998;135:319-23)
- **Epilepsy:** Vitamin D deficiency can cause seizures. Medications used to treat epilepsy commonly cause vitamin D deficiency, which can then result in iatrogenic epilepsy (Ali FE, et al. *Ann Pharmacother* 2004;38:1002-5). Administration of vitamin D shows an anticonvulsant benefit (Christiansen C, et al. *Br Med J.* 1974;2:258-9).
- **Polycystic ovary syndrome:** Vitamin D deficiency was highly prevalent among 13 women with PCOS, and supplementation with 1,500 mg of calcium per day and 50,000 IU of vitamin D2 on a weekly basis normalized menstruation and/or fertility in nine of nine women with PCOS-related menstrual irregularities within three months of treatment (Thys-Jacobs S, et al. *Steroids* 1999;64:430-5)
- **Osteoarthritis and musculoskeletal pain:** Osteoarthritis develops more frequently and progresses more rapidly in patients who are deficient in vitamin D. Vitamin D deficiency is alarmingly common in patients

with musculoskeletal pain (Plotnikoff GA, Quigley JM. *Mayo Clin Proc.* 2003;78:1463-70). Treatment of patients with back pain and hypovitaminosis D with 5,000 – 10,000 IU per day of vitamin D results in alleviation of pain in almost 100% of patients (Al Faraj S, Al Mutairi K. *Spine.* 2003;28:177-9)

- **Inflammatory and autoimmune diseases:** Vitamin D deficiency is common in patients with various autoimmune diseases such as Grave's disease, lupus, rheumatoid arthritis, and ankylosing spondylitis. Vitamin D administration to children (2,000 IU per day) was shown to reduce the incidence of immune-mediated type 1 diabetes by 80% (Hypponen E, et al. *Lancet* 2001 Nov 3;358:1500-3). Preliminary evidence shows that vitamin D administration has a beneficial clinical and anti-inflammatory effect in patients with multiple sclerosis (Goldberg P, et al. *Med Hypotheses* 1986;21:193-200 and Mahon BD, et al. *J Neuroimmunol.* 2003;134:128-32)

We recently proposed that optimal vitamin D status is defined by serum levels of 25(OH) vitamin D in the range of 40 to 65 ng/mL (100 - 160 nmol/L). This proposal was based on our clinical experience and our extensive review of the literature, particularly the recent publications by Vieth (*Am J Clin Nutr* 1999;69:842-56), Zitterman (*Br J Nutr* 2003;89:552-72), Holick (*Am J Clin Nutr* 2004;79:362-71), and Heaney et al (*Am J Clin Nutr* 2004;79:362-71). Our proposal is graphically illustrated in Figure 1 to help clinicians interpret results of serum testing and apply this information clinically.

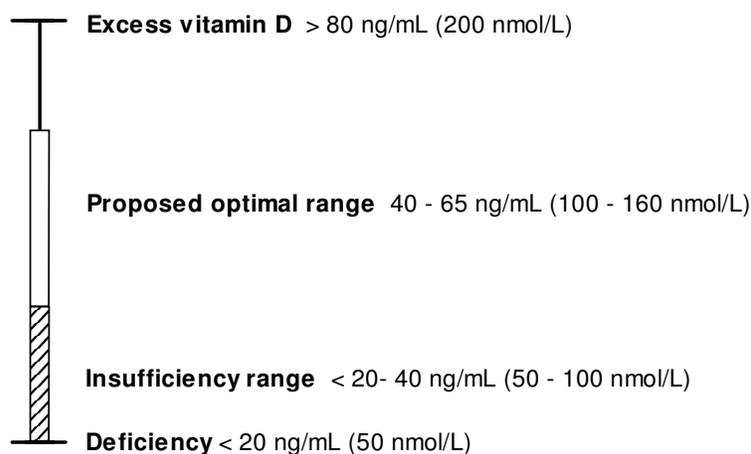


Figure 1. Proposed normal and optimal ranges for serum 25(OH)D levels based on current research. Modified from Vasquez, *Integrative Orthopedics*, 2004 with permission.

Safe and effective implementation of vitamin D therapy necessitates three components: 1) identification of patients who are vitamin D deficient or who have a vitamin D-responsive condition, 2) administration of vitamin D with oral supplementation in the range of 1,000 IU per day for infants, 2,000 IU per day for children and 4,000 IU per day for adults, and 3) periodically monitoring 25(OH)D levels and serum calcium to ensure efficacy and safety, respectively. Dr Mercola has discussed vitamin D extensively on his website, and based on his experience in testing and treating more 2,000 patients with vitamin D deficiency, he concluded that emulsified vitamin D—specifically Bio-D-Mulsion from Biotics Research Corporation—provided superior clinical responses; his discussion of this topic is located at <http://www.mercola.com/forms/vitamind.htm>. Additional information and references are available in our other publications on this topic (Vasquez, Manso, Cannell. *Altern Ther Health Med*, in press) and in a recent textbook on integrative orthopedics (Vasquez A. *Integrative Orthopedics: The Art of Creating Wellness While Effectively Managing Acute and Chronic Musculoskeletal Injuries*, www.OptimalHealthResearch.com: 2004).

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