

Toxicity of Vitamin D

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Toxicity

Isn't vitamin D toxic? Not if we take the same amount nature intended when we go out in the sun. ^[1] Vieth attempted to dispel unwarranted fears in medical community of physiological doses of vitamin D in 1999 with his exhaustive and well-written review.

His conclusions: fear of vitamin D toxicity is unwarranted, and such unwarranted fear, bordering on hysteria, is rampant in the medical profession. ^[2] Even Ian Monroe, the chair of the relevant IOM committee, wrote to the Journal to compliment Vieth's work and to promise his findings will be considered at the time of a future Institute of Medicine review. ^[3] That was more than two years ago.

In 1999, Vieth indirectly asked the medical community to produce any evidence 10,000 units of vitamin D a day was toxic, saying, "Throughout my preparation of this review, I was amazed at the lack of evidence supporting statements about the toxicity of moderate doses of vitamin D". He added, "If there is published evidence of toxicity in adults from an intake of 250ug (10,000 IU)/d, and that is verified by the 25(OH)D concentration, I have yet to find it." 1

Like most medication, cholecalciferol is certainly toxic in excess, and, like Coumadin, is used as a rodent poison for this purpose. Animal data indicates signs of toxicity can occur with ingestion of .5mg/kg (20,000 IU/kg), while the oral LD⁵⁰ (the dose it takes to kill half the animals) for cholecalciferol in dogs is about 88 mg/kg (3,520,000 IU/kg).^[4]

This would be equivalent to a 110-pound adult taking 176,000,000 IU or 440,000 of the 400 unit cholecalciferol capsules! Vieth reports human toxicity probably begins to occur after chronic daily consumption of approximately 40,000 IU a day (100 of the 400 IU capsules).¹ Heavy sun exposure, when combined with excessive supplement use is a theoretical risk for vitamin D toxicity, but if such a case has been reported, I am not aware of it.

Physician ignorance about vitamin D toxicity is widespread. A case report of four patients appeared in the 1997 Annals of Internal Medicine, accompanied by an editorial warning about vitamin D toxicity.^{[5], [6]} However, careful examination of the patients reveals that both papers are a testimony to the fact that incompetence about vitamin D toxicity can reach the highest levels of academia.^{1, [7]} See our "Worst papers on vitamin D" section for a full critique.

Although there are documented cases of pharmacological overdoses from ergocalciferol, the only documented case of pharmacological, not industrial, toxicity from cholecalciferol we could find in the literature was intoxication from over-the-counter supplement called Prolongevity.^[8] On closer inspection, it seemed more like an industrial accident but is interesting because it gives us some idea of the safety of cholecalciferol. The capsules consumed contained up to 430 times the amount of cholecalciferol contained on the label (2,000 IU). The man had been taking between 156,000 to 2,604,000 IU of cholecalciferol a day (equivalent to between 390 and 6,500 of the 400 unit capsules) for two years. He recovered uneventfully after the proper diagnosis, treatment with steroids and sunscreen.

It is true that a few people may have problems with high calcium due to undiagnosed vitamin D hypersensitivity syndromes such as primary hyperparathyroidism, granulomatous disease or occult cancers but a blood calcium level, a PTH, a 25(OH)D and calcitriol level should help clarify the cause of the hypersensitivity. Although D can be toxic in excess, the same can be said for water.

As a physician, I know that psychotic patients should drink about eight glasses of water a day. However, many would hurt themselves by regularly drinking 40 glasses a day (called compulsive water intoxication). So you could say that water has a therapeutic index of five (40/8).

Heaney's recent research indicates that healthy humans utilize about 4,000 units of vitamin D a day (from all sources).⁷ However, 40,000 units a day will hurt them (over several years).¹ Therefore, vitamin D has a therapeutic index of 10 (40,000/4,000), twice as safe as water. Although we are not saying it is as safe as water, we are saying vitamin D is safe when used in the doses nature uses it.

The single most important fact anyone needs to know about vitamin D is how much nature supplies if we behave naturally, e.g., go into the sun. Humans make at least 10,000 units of vitamin D within 30 minutes of full body exposure to the sun (minimal erythemal dose).^[9] Vitamin D production in the skin occurs within minutes and is already maximized before your skin turns pink.

Fear of the fatal form of skin cancer, malignant melanoma, keeps many people out of the sun. The problem with the theory is that the incidence of melanoma continues to increase dramatically although many people have been completely avoiding the sun for years.^[10] We are not saying sunburns are safe, they are not. We are saying that brief full body sun exposure (minimal erythemal doses) may slightly increase your risk of skin cancer but it is a much smarter thing to do than dying of vitamin D deficiency.

Vitamin D hypersensitivity syndromes are often mistaken for vitamin D toxicity. The most common is primary hyperparathyroidism. Other syndromes occur when abnormal tissue subverts the kidney's normal regulation of endocrine calcitriol production. Aberrant tissues, usually granulomatous, convert 25(OH)D into calcitriol causing high blood calcium. The most common such condition is sarcoidosis, oat cell carcinoma of the lung and non-Hodgkin's lymphoma but other illness can cause the syndrome and they can occur while the patient's 25(OH)D levels are normal or even low. For that reason, while rare, it is advisable to seek a knowledgeable physician's care when repleting your vitamin D system, especially if you are older, have sarcoidosis, cancer or other granulomatous diseases. In such high-risk patients, periodic monitoring of 25(OH)D levels and serum calcium will alert the physician to the need to do more tests, such as calcitriol or PTH, and take further action.

However, it seems clear that restoring physiological serum levels of 25(OH)D will help many more patients than it will hurt. In fact, living in America today while worrying about vitamin D toxicity is like dying of thirst in the desert while worrying about drowning.

- [1] [Vieth R. Vitamin D supplementation, 25-hydroxyvitamin D concentration, and safety. Am J Clin Nutr. 1999;69:842-56.](#)
- [2] [Vieth R; Chan PC; MacFarlane GD, Efficacy and safety of vitamin D3 intake exceeding the lowest observed adverse effect level. Am J Clin Nutr 2001 Feb;73\(2\):288-94](#)
- [3] [Munro I, Derivation of tolerable upper intake levels of nutrients, Letter, Am J Clin Nutr 2001; 74:865](#)
- [4] [An Overview of Cholecalciferol Toxicosis, The American Board of Veterinary Toxicology \(ABVT\)](#)
- [5] [Adams JS, Lee G. Gains in bone mineral density with resolution of vitamin D intoxication. Ann Intern Med. 1997 Aug 1;127\(3\):203-6.](#)
- [6] [Marriott BM. Vitamin D supplementation: a word of caution. Ann Intern Med. 1997 Aug 1;127 \(3\):231-3.](#)
- [7] [Heaney R, Davies K, Chen T, Holick M, Barger-Lux MJ. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. Am J Clin Nutr 2003;77:204-10.](#)
- [8] [Koutkia P, Chen TC, Holick MF. Vitamin D intoxication associated with an over-the-counter supplement. N Engl J Med. 2001 Jul 5;345\(1\):66-7.](#)
- [9] [Holick MF. Environmental factors that influence the cutaneous production of vitamin D. Am J Clin Nutr. 1995 Mar;61\(3 Suppl\):638S-645S.](#)

[10] [Hemminki K, Zhang H, Czene K. Incidence trends and familial risks in invasive and in situ cutaneous melanoma by sun-exposed body sites. Int J Cancer. 2003 May 10;104\(6\):764-71](#)