

# Vitamin D: Deficiency, Diversity and Dosage

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*Vitamin D deficiency is a major unrecognized health problem.* - Michael F. Holick, M.D., Boston University Medical Center

There have been many papers published on vitamin D. A Medline search for “vitamin D” will yield over 32,000 matches. It is well established that insufficient quantities of the vitamin contribute to osteopenia, osteomalacia, and osteoporosis. However, there is so much new interest in “boneless” applications of vitamin D that the topic was featured in the June, 2003 *Reader's Digest*.<sup>1</sup>

## Introduction

Vitamin D was first isolated from tuna fish oil in 1936, and synthesized in 1952. It is a prohormone sterol which the body manufactures, given sunlight, from 7-dehydrocholesterol. Vitamin D3 (C<sub>27</sub>H<sub>44</sub>O, cholecalciferol) is the form we and other animals make, and what is found in fish liver oil. Oddly enough, fish cannot synthesize vitamin D. They get theirs low on the food chain from planktonic algae; big fish eat little fish; we eat big fish.

Vitamin D2 (C<sub>28</sub>H<sub>44</sub>O) is made from ergosterol, not cholesterol, and consequently is called ergocalciferol. This is the form that is found in plants. Vitamin D2 man-made by ultraviolet irradiation of ergosterol is the form usually added to milk and found in most American supplements. Vitamin D3 is more commonly used as a supplement in Europe.<sup>2</sup> As a curiosity, reindeer lichen contains both vitamin D2 and D3.<sup>3</sup>

Although D2 and D3 differ by a single carbon atom, there is evidence that D3 is more efficiently utilized in chicks<sup>4</sup> and, more to the point, in humans. “The assumption that vitamins D2 and D3 have equal nutritional value is probably wrong and should be reconsidered.”<sup>5</sup>

There are two commercial sources of natural vitamin D3: fish liver oil and an oil extracted from wool. “If a label lists ‘vitamin D3 (cholecalciferol)’ then it is from wool oil. This is considered a vegetarian source (the animal is not harmed, just sheared), but not vegan. Fish liver oil will be in parentheses if it is the source.”<sup>6</sup> Animals can obtain vitamin D from licking their fur, and in humans, rickets can be successfully treated by rubbing cod liver oil into the skin.

## Long-Term Safety

As with all vitamins, there is ongoing and ever-protracted debate about vitamin D's safety and effectiveness. In the end, the issue really boils down to dosage. Because vitamin D can be made in the body, given sufficient sunlight, it has been considered more of a hormone than a vitamin. This terminology is likely to prejudice any consideration of megadoses, and that is unfortunate. Government-sponsored “tolerable” or “safe upper limits” (UL) for vitamin D have been established, perhaps based as much on speculation as on available facts. For babies under one year, the UL is 1,000 IU (25 mcg) per day. For everyone else, including pregnant and nursing women, it is 2,000 IU (50 mcg) per day.<sup>7</sup> These “safe upper limits” may be conservative. Vieth et al. write, “The 100 mcg/day (4,000 IU/day) dosage of vitamin D3 effectively increased 25(OH)D to high-normal concentrations in practically all adults and serum 25(OH)D remained within the physiologic range; therefore, we consider 100 mcg vitamin D3/day (4,000 IU/day) to be a safe intake.”<sup>8</sup>

Vitamin D has sometimes been regarded as the most potentially dangerous vitamin. In his 2001 article “Vitamin Toxicity,” Mark Rosenbloom, M.D., writes that, for vitamin D, “Acute toxic dose is not

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established, and chronic toxic dose is more than 50,000 IU/day in adults. In children, 400 IU/day is potentially toxic. A wide variance in potential toxicity exists." There were no fatalities cited.<sup>9</sup>

The Merck Manual's assessment is somewhat different: "Vitamin D 1000 mcg (40,000 IU)/day produces toxicity within 1 to 4 months in infants, and as little as 75 mcg (3,000 IU)/day can produce toxicity over years. Toxic effects have occurred in adults receiving 2,500 mcg (100,000 IU)/day for several months."<sup>10</sup>

The Merck Manual's lowest "toxicity" figure for "infants" of 3,000 IU is substantially higher than Rosenbloom's "potentially toxic" figure of 400 IU for presumably older and larger "children." "Potentially toxic" is very different from "toxic." Moreover, "toxic" is very different from "death." The choice to use the word "toxic" may serve to convey a false impression of immediate and mortal danger. There are numerous symptomatic warnings before serious toxic effects occur. Merck says, "The first symptoms are anorexia, nausea, and vomiting, followed by polyuria, polydipsia, weakness, nervousness, and pruritus. (Eventually) renal function is impaired...Metastatic calcifications may occur, particularly in the kidneys. In Great Britain, so-called hypercalcemia in infancy with failure to thrive has occurred with a daily vitamin D intake of 50 to 75 mcg (2,000 to 3,000 IU)."<sup>10</sup> Though the details and duration of intake are not stated, a body-weight comparison suggests that if an infant weighed 10 pounds, that would be the dose equivalent of approximately 32,000 to 48,000 IU per day for an average adult.

A widely-used nutrition textbook that I taught from said that anything over 2,000 IU daily for an adult is toxic.<sup>11</sup> In this same textbook, on the same page, there was an error that, by the author's own standard, could likely be fatal to the reader's baby. A "Caution" statement on page 221 indicated the daily vitamin D requirement for an infant as 10 *milligrams*. This is 1,000 times

the correct figure, which is 10 micrograms. 10 milligrams is 400,000 IU; 10 micrograms is 400 IU. That textbook typo is a far greater mistake than any health enthusiast would ever make. By the next edition, the mistake had been corrected.

This is not an isolated instance. As recently as July, 2003, the website of a major university medical school made the same mistake of stating milligrams (mg) instead of micrograms (mcg). This abbreviation error, amounting to a difference of three orders of magnitude, was present no fewer than six times in a single article. One of the medical school's statements read, "The upper limit of safety for vitamin D established by the Food and Nutrition Board of the Institute of Medicine is 25 mg (1000 IU) daily for infants and 50 mg (2000 IU) for children and adults." Actually, 25 mg would be one million IU/day, and 50 mg is two million IU/day. Mark Twain's advice comes to mind: "Be careful in reading health books. You may die of a misprint." The error has since been corrected.<sup>12</sup>

Perhaps it is a testament to the safety of vitamin D that there has never been a report of any reader deaths from medical school-induced hypervitaminosis. Additionally, if nutrition textbook and medical school proofreaders can confuse milligrams with micrograms, then certainly the public can. This may serve as a practical example of the advantage of using International Units in discussing and labelling the fat-soluble vitamins.

It is instructive to note that as far back as 1939, some truly enormous doses of vitamin D were in fact found to be far less deadly than one might expect. In several countries, most infants, including those prematurely born, survived 200,000 to as many as 600,000 units of vitamin D given in a single injected or oral dose. These are incredibly high quantities, especially when they are considered in relation to a premature infant's body weight.<sup>13</sup> Pregnant women have likewise been given two huge

oral doses of vitamin D (600,000 IU) during the 7th and 8th months.<sup>14</sup>

In 2003, vitamin D's safety margins appear pretty much unchanged. This year, the British Medical Journal published a double-blind controlled trial of 100,000 IU vitamin D3 given orally to over 2,000 elderly patients once every four months, for five years. The authors reported, in addition to greatly reduced fracture rates, that the high-dose therapy was "without adverse effects in men and women."<sup>15</sup>

It may readily be conceded that huge but occasional doses are insufficient to produce toxicity because vitamin D is fat-soluble, stored by the body, and it takes many months of very high doses to produce calcification of soft tissues, such as the lung and kidneys. "Overdose," "toxic," and "fatal" are very strong, yet very different terms that are often used interchangeably by critics of vitamin supplementation. Most overdoses are not toxic, and most toxicities are not fatal. Current US Daily Reference Intakes (DRI) for vitamin D are:

Infants 0-12 months, 200 IU (5 mcg)  
Males and females 1-50 years, 200 IU (5 mcg)  
51-70 years, 400 IU (10 mcg)  
71 years and older, 600 IU (15 mcg)  
Pregnant or nursing women, 200 IU (5 mcg)<sup>7</sup>

Formerly, the US RDA for vitamin D was only 5 mcg (200 IU) for older adults. The present recommendations are an improvement. However, there is evidence that even three times the DRI for an adult is inadequate if a person is not receiving adequate sunlight.<sup>16</sup> DRI or RDA levels are certainly not therapeutic levels, as the treatment of rickets generally requires a dose of 1,600 IU/day, and may require a daily dosage of 50,000 to as much as 300,000 IU in resistant cases.<sup>17</sup>

Current widely-publicized government recommendations are probably inadequate for disease prevention. Reinhold Vieth, Ph.D., writes, "For adults, the 5-microgram (200 IU) vitamin D recommended dietary allowance may prevent osteomalacia in the

absence of sunlight, but more is needed to help prevent osteoporosis and secondary hyperparathyroidism. Other benefits of vitamin D supplementation are implicated epidemiologically: prevention of some cancers, osteoarthritis progression, multiple sclerosis, and hypertension. Total-body sun exposure easily provides the equivalent of 250 mcg (10,000 IU) vitamin D/day, suggesting that this is a physiologic limit. Except in those with conditions causing hypersensitivity, there is no evidence of adverse effects with serum 25(OH)D concentrations <140 nmol/L, which require a total vitamin D supply of 250 mcg (10,000 IU)/day to attain. Published cases of vitamin D toxicity with hypercalcemia, for which the 25(OH)D concentration and vitamin D dose are known, all involve intake of greater than or equal to 1,000 mcg (40,000 IU)/day. Because vitamin D is potentially toxic, intake of >25 mcg (1,000 IU)/day has been avoided even though the weight of evidence shows that the currently accepted, no observed adverse effect limit of 50 mcg (2,000 IU)/day is too low by at least 5-fold."<sup>18</sup>

These figures, high though they may seem, may actually be fairly conservative. *The Nutrition Desk Reference, 2nd Edition*<sup>19</sup> states that, for vitamin D, "The threshold for toxicity is 500 to 600 mcg per kilogram body weight per day." (p.40) "Toxic" in this particular instance must mean "death," as this figure is presumably based on the US Environmental Protection Agency's published oral LD50 for female rats of 619 mg/kg.<sup>20</sup> 500 to 600 mcg is the equivalent of 20,000 to 24,000 IU per kilogram body weight per day. By comparison, this would mean that for an average (70 kg) adult human, toxicity would occur at an astounding 1,400,000 to 1,680,000 IU/day. In ducks, it is even higher: EPA's LD 50 for mallards is greater than 2000 mg/kg, more than three times that for female rats.

Even if such figures were not directly applicable to human beings, vitamin D must remain one of the most non-toxic

substances imaginable. It might be speculated that at least some of the recent increase of interest in vitamin D analogs is due, in part, to patent- and profit-driven attempts to chemically sidestep the presumed dangers of high doses of inexpensive, natural vitamin D. If the vitamin is non-toxic, incentive to develop pharmaceutical analogs largely disappears.

There are, of course, some reasonable cautions with its use. Persons with hyperparathyroidism, lymphoma, lupus erythematosus, tuberculosis, sarcoidosis, kidney disease, or those taking digitalis, calcium channel-blockers, or thiazide diuretics, should have physician supervision before and while taking extra vitamin D. Hyperparathyroidism has been successfully managed with 50,000 to 200,000 IU of vitamin D daily.<sup>21</sup> When employing large doses of vitamin D, periodic testing is highly advisable.

### Deficiency

Vitamin D deficiency may be found in people who do not take supplements, who receive little sun exposure, and who do not drink vitamin D fortified milk. A recent study<sup>22</sup> indicates that about a quarter of supposedly bone-growing American adolescents are likely vitamin D deficient. "Additionally, phenytoin (Dilantin), primidone (Mysoline), and phenobarbital for seizures; corticosteroids; cimetidine (Tagamet) for ulcers; the blood-thinning drug heparin; and the antituberculosis drugs isoniazid (INH) and rifampin may interfere with vitamin D absorption or activity."<sup>23</sup> Cyclosporine and carba-mazepene also negatively interfere with vitamin D. Vitamin D deficiency is prevalent in the elderly, who all too commonly have poor diets, take the most medication, and get the least sunlight. Furthermore, the normal aging process itself decreases the body's ability to make vitamin D from what sunlight may be received. In any age group, even a relatively wholesome-appearing diet heavy in cereal grains reduces the availability of vitamin D in the body.<sup>24</sup>

### Osteoporosis

For decades, a milk-fed (and dairy industry-educated) public has had its attention focused on calcium and largely diverted from the "other" important osteoporosis-preventing factor: vitamin D. Not only is vitamin D necessary for calcium deposition in the body, it is necessary for getting calcium into the body in the first place. "(P)assive diffusion (dictated by calcium intake) is not the major mechanism by which dietary calcium is absorbed by normal adult humans. The vitamin D-dependent processes are more important quantitatively and thus constitute a major determinant of calcium status. Individuals who are not exposed to sunlight may be especially at risk."<sup>25</sup>

Most persons with osteoporosis have low vitamin D levels. Along with calcium, 800 IU of vitamin D daily has been shown in a double-blind, placebo-controlled study to increase bone density, and to reduce hip fractures by an astounding 43%.<sup>26</sup> Fractures and their complications are a major cause of death in the elderly. Up to "27% of all hip fracture victims die within six months of their fall, usually of complications following surgery or from infections."<sup>27</sup> There are over 250,000 hip fractures annually among persons over age 65, and probably "90% of all fractures past age 60 are due to osteoporosis."<sup>28</sup> Vitamin D therapy can save lives as well as bones. The fact that the DRI of vitamin D is tripled for the elderly is an indication that this fact is not unknown. But 600 IU of vitamin D for a 71 year old is probably too little, and for some, too late.

Such was nearly the case for my mother, a grand mal epileptic who took phenytoin (Dilantin) for nearly 50 years. As she aged, she began to fracture easily. This problem continued even after she was put on calcium supplements accompanied by an RDA-level vitamin D supplement. But after her vitamin D intake was raised to 2,000 IU/day, she never broke a bone again. This is true even though she still fell from

time to time, sometimes so severely that she required inpatient care. But there were no more fractures. Epileptics may need as much as 4000 IU daily.<sup>29</sup> "Interestingly, vitamin D may offer another benefit for osteoporosis: studies have found that when older individuals take vitamin D supplements, they have less of a tendency to sway while standing or walking, and may therefore be less likely to fall."<sup>23</sup>

### Rickets

Childhood rickets remains a larger public health problem than might be expected. "Until recently, rickets secondary to vitamin D deficiency was considered a medical oddity rather than a clinical reality in Catalonia (Spain). However, recent data show a re-emergence of the disease in infancy. Nutritional rickets...mainly affects immigrant infants and children from Sub-Saharan Africa and Morocco, black or dark-skinned, fed with maternal milk alone, without vitamin D supplementation and with little sun exposure. Systematic, preventive supplementation with vitamin D is essential in these populations."<sup>30</sup>

Such is the case elsewhere as well. On the sunny island of Crete, "A full-term male infant presented with clinical and biochemical findings consistent with the diagnosis of congenital rickets: weak muscle tone, craniotabes, episodes of tremor, hypocalcaemia, elevated serum alkaline phosphatase, secondary hyperparathyroidism, decreased 25-hydroxyvitamin D and normal 1,25-dihydroxyvitamin D serum levels. The mother's history and biochemical findings suggested nutritional vitamin D deficiency...It is surprising that this case occurred in an affluent setting, in the Mediterranean island of Crete, with an abundance of sunlight throughout the year." The authors assert that "a high index of suspicion is required for prompt diagnosis and treatment, thus preventing complications."<sup>31</sup> Seizures may be a symptom of rickets.<sup>32,33,34</sup>

"A high index of suspicion" of vitamin

D deficiency would be a good policy for clinicians in the United States as well. Rickets has been observed in Texas<sup>35</sup> and in North Carolina, where "Thirty patients with nutritional rickets were first seen between 1990 and June of 1999. Over half of the cases occurred in 1998 and the first half of 1999. All patients were African American children who were breast fed without receiving supplemental vitamin D... Factors that may have contributed to the increase in referrals of children with nutritional rickets include more African American women breast-feeding, fewer infants receiving vitamin D supplements, and mothers and children exposed to less sunlight. We recommend that all dark-skinned breast-fed infants and children receive vitamin D supplementation."<sup>36</sup>

Heavily pigmented skin blocks up to 95% of UV radiation to the deepest skin layers. Additionally, now-widespread air pollution interferes with vitamin D synthesis in two almost paradoxical ways. Particulate pollution reduces the amount of sunlight people may receive, and ozone depletion causes people to minimize exposure to what sunlight there is. As people are cover their skin to avoid skin cancer, they reduce their vitamin D.

On August 4, 2002, Reuters News Service reported that "the number of cases of rickets in the United States has crept up in recent years. Breast milk contains many valuable nutrients but not enough vitamin D to meet the daily requirement of 200 IU. Exposure to the sun's rays normally generates Vitamin D in the skin, but applying sun block stops that process."

### Food Fortification

With the exception of oily fish, foods do not contain a significant amount of vitamin D. Because of concern over mercury levels, eating the flesh of fish may not be practical advice, and, while it contains no mercury, there is widespread dislike for cod liver oil. Since the 1930s, vitamin D has been added to milk but not to other milk

products. More recently, it has also been added to flour to reduce rickets among immigrants to Britain.<sup>10</sup>

It is cheap and reliable for people to get their vitamin D from enriched foods. Iodine, iron and some of the B-vitamins are other examples of nutrients that have been added to foods for decades. That action should be seen for what it is: a national policy effectively acknowledging that the masses eat so inadequately that they are otherwise unable to avoid the most obvious clinical ramifications of the most classic of nutrient deficiencies, including iodine-deficiency goiter, iron-deficiency anemia, and pellagra. In the case of vitamin D, it is a tacit statement about safety as well. With 400 IU added per quart, it is easy for many a milk-drinking teenager to easily quadruple the DRI of 200 IU/day. Few dietitians appear worried that many people are routinely and substantially exceeding government DRIs for vitamin D.

Adding fluoride to public water supplies is a similar, if less well reasoned, application of government intervention. There has been nearly as much interest in trying to strengthen bones with fluoride as there has been in using vitamin D. But not only does fluoridation fail to protect bones from fracture, it actually contributes to increased fractures.<sup>37,38</sup>

Additionally, both the National Toxicology Program and the National Cancer Institute found a fluoride-related increase in osteosarcoma in young males.<sup>39</sup> Water fluoridation isn't particularly effective in preventing dental caries, resulting in an average of one half of one filling less per user per lifetime.<sup>40</sup>

### Obesity

Supplements, not sunlight, may be necessary for overweight persons because they are less than half as able to utilize cutaneously-synthesized vitamin D3 compared to lean persons. Since approximately two-thirds of all Americans are overweight or obese, this is a very significant public health problem. "In the obese subjects oral

vitamin D was more bioavailable than vitamin D from sunlight exposure...The authors propose that vitamin D is being sequestered in body fat in obese persons, giving rise to a relative deficiency which could be corrected with oral administration of extra vitamin D."<sup>41</sup>

### Diversity of Uses

Controversy over vitamin D therapy increases with the distance research moves away from the skeleton. There is growing evidence that the "sunshine vitamin" may be vastly more important to human health than previously thought and commonly taught. Vitamin D metabolite (1,25-dihydroxyvitamin D) receptors, writes Michael F. Holick, M.D., "are present not only in the intestine and bone, but in a wide variety of other tissues, including the brain, heart, stomach, pancreas, activated T and B lymphocytes, skin, gonads, etc. 1,25(OH)(2)D is one of the most potent substances to inhibit proliferation of both normal and hyperproliferative cells and induce them to mature...Chronic vitamin D deficiency may have serious adverse consequences, including increased risk of hypertension, multiple sclerosis, cancers of the colon, prostate, breast, and ovary, and type 1 diabetes."<sup>42</sup>

It is noteworthy that skin cancer may actually be prevented by what many feel causes it: sunshine.<sup>43,44</sup> Krispin Sullivan, author of *Naked at Noon: Understanding Sunlight and Vitamin D*, writes: "One of the known protectors of skin cells from pre-cancerous changes is vitamin D. For most Americans the primary source of vitamin D is sunlight. UV-B, the only band of light producing vitamin D, is significantly present only midday during summer months in most of the U.S., the exact time we are advised to avoid sunlight. UV-B is blocked by sunscreen."<sup>45</sup> Over-exposure to sunlight does not cause vitamin D toxicity. Persisting concerns over sun exposure are arguments in favor of its nutritional equivalent: oral vitamin D supplementation.

## Multiple Sclerosis

Persons with multiple sclerosis typically are vitamin D deficient and demonstrate dramatically reduced bone mass. Not surprisingly, such bone loss appears to be directly caused by insufficient vitamin D<sup>46</sup> and can “be safely and inexpensively corrected by the routine use of vitamin D supplements.”<sup>47</sup>

More importantly, vitamin D may have a key role in the progression of multiple sclerosis itself. Hayes et al. write, “(E)xogenous 1,25-dihydroxyvitamin D<sub>3</sub>, the hormonal form of vitamin D<sub>3</sub>, can completely prevent experimental autoimmune encephalomyelitis (EAE), a widely accepted mouse model of human multiple sclerosis (MS)...(T)he hormonal form of vitamin D<sub>3</sub> is a selective immune system regulator inhibiting this autoimmune disease. Thus, under low-sunlight conditions, insufficient vitamin D<sub>3</sub> is produced, limiting production of 1,25-dihydroxyvitamin D<sub>3</sub>, providing a risk for MS...This theory can explain the striking geographic distribution of MS, which is nearly zero in equatorial regions and increases dramatically with latitude in both hemispheres...MS may be preventable in genetically susceptible individuals with early intervention strategies that provide adequate levels of hormonally active 1,25-dihydroxyvitamin D<sub>3</sub> or its analogs.”<sup>48</sup> Hayes adds that “Inheriting genetic risk factors for multiple sclerosis (MS) is not sufficient to cause this demyelinating disease of the central nervous system; exposure to environmental risk factors is also required.”<sup>49</sup>

In a review article, “Vitamin D Supplementation in the Fight Against Multiple Sclerosis,”<sup>50</sup> Ashton F. Embry credits P. Goldberg<sup>51, 52</sup> with being the first to propose that vitamin D is an important factor in the development of MS. Goldberg “postulated that such a close correspondence between low sunlight and MS was due to low vitamin D production in the population. Goldberg also showed that within areas of

low sunlight (e.g. Norway) differences in MS prevalence could be explained by dietary factors which affect vitamin D production. Such factors include the amount of fish eaten (increases vitamin D) and the amount of grains consumed (reduces vitamin D levels due to the action of phytates). To explain how vitamin D levels were related to MS, Goldberg proposed that genetically susceptible individuals may need larger than normal amounts of vitamin D during myelin formation and that insufficient vitamin D during childhood might result in defective myelin which would be susceptible to breakdown in later life. Goldberg’s ideas were completely ignored by medical researchers.”

At least at the time they were. Eventually it was demonstrated that vitamin D hormone could prevent or halt not only an animal form of MS<sup>53,54</sup> but there had been a clinical study<sup>55</sup> showing that vitamin D, along with calcium and magnesium, reduced the relapse rate in humans with multiple sclerosis. Frederick R. Klenner, M.D., reported success using vitamin and mineral therapy for multiple sclerosis over thirty years ago.<sup>56,57,58</sup>

## Heart Disease and Other Clinical Uses

Vitamin D has an important role in cardiovascular health.<sup>59,60</sup> For example, not only can it prevent hypertension, it can help treat it.<sup>61,62</sup> “Hypertension appears to improve with vitamin D supplementation whether or not the vitamin is deficient.”<sup>63</sup> This is an important point.

Congestive heart failure (CHF) may be caused by vitamin D deficiency. “Low vitamin D status can explain alterations in mineral metabolism as well as myocardial dysfunction in the CHF patients, and it may therefore be a contributing factor in the pathogenesis of CHF.”<sup>64</sup> Not surprisingly, bone loss is associated with congestive heart failure.<sup>65</sup> Dilated cardiomyopathy has been linked with rickets, both of which “responded well to supplemental calcium and vitamin D.”<sup>66</sup>

Scleroderma has responded favorably to long term oral vitamin D3 (1,25-dihydroxycholecalciferol) therapy<sup>67</sup> and psoriasis has been successfully treated, not only with vitamin D analogues, but with topical vitamin D3.<sup>68</sup> Vitamin D deficiency may be a contributing cause of inflammatory bowel disease, and might be an effective treatment.<sup>69</sup> Over 50 years ago, lupus vulgaris (tuberculosis of the skin) was reported successfully treated with 150,000 IU of vitamin D daily for six to eight months.<sup>70</sup>

Colon cancer is clearly related to poor vitamin D nutrition.<sup>71,72,73</sup> Inadequate vitamin D levels are also associated with ovarian cancer,<sup>74</sup> polycystic ovary syndrome,<sup>75</sup> rheumatoid arthritis,<sup>76</sup> and lupus.<sup>77</sup> Infants receiving vitamin D supplements show as much as an 80% reduction in type I diabetes.<sup>78-81</sup> A Medline search will reveal nearly 300 papers on fighting prostate cancer with vitamin D and its derivatives, and nearly 400 in relation to D and breast cancer.

### Deficiency and Diversity: A Summary

Vitamin D deficiency is cause or contributor to a wide variety of diseases, many of which appear unrelated to bone problems. So important is this vitamin for the entire population that it is necessary for milk to be enriched with it. Most persons do not get adequate vitamin D from sunlight, and the problem is compounded for the obese and for the elderly. For those individuals, and for any person on any of a number of commonly prescribed medications, vitamin D supplementation is mandatory.

Government recommended dietary intakes of 200 to 600 IU/day are too low, according to the weight of clinical evidence. Government "tolerable" or "safe upper intake levels" (UL) of 1,000 to 2,000 IU/day are likewise too low, and largely unsupported by toxicological evidence. An optimum health recommendation of 1,000 to 4,000 IU/day, in total from all sources, is not unreasonable for the vast majority of healthy adults. Effective therapeutic levels for illness may

be much higher. When high doses are used, appropriate testing and monitoring is recommended. It would be unreasonable to deny a therapeutic trial of vitamin D in cases of multiple sclerosis, scleroderma, psoriasis, congestive heart failure, hypertension, and various forms of cancer.

Excessive avoidance of sunlight, and sensational but unscientific dread of relatively high-dose vitamin D side effects does more than merely set the stage for a population of rickety children and fracture-ridden elderly. Overestimates and outright misstatements of vitamin D's "potential toxicity" open new marketing avenues for the development of vitamin D-like drugs, a commercial opportunity that the pharmaceutical industry has not overlooked.

### On Dangers and Dosage: A Concluding Comment

Hypervitaminosis articles are popular with the media, sometimes even making it into the pages of the *Wall Street Journal*. On April 30, 1992, David Stipp reported that between 1990 and 1992, "a series of patients with vitamin D overdoses began turning up at Boston hospitals." One of these patients subsequently died from drug complications, and the case went to court.<sup>82</sup> "Essentially, this was a product liability action against the producer of dairy products, specifically milk which contained excessive amounts of vitamin D. The plaintiff's decedent purportedly suffered from elevated levels of vitamin D in her bloodstream which required medication which in turn allegedly compromised her immune system, leading to her death."<sup>83</sup> This is the one and only vitamin D-related death I could find confirmation of anywhere, and even this one was not directly due to the vitamin, but rather to side effects of medication.

A physiology textbook later stated that "At least 19 cases of vitamin D toxicity were reported in the Boston area during 1992. Symptoms included fatigue, weight loss, and potentially severe damage to the kid-



neys and cardiovascular system. The problems resulted from drinking milk fortified with vitamin D. Due to problems at one dairy, some of the milk sold had over 230,000 units of vitamin D per quart instead of the usual 400 units per quart. The incident highlighted the need for quality control in the production, and care in the consumption, of vitamin supplements.”<sup>84</sup>

Such a conclusion is inaccurate. The incident might just as well be taken to be an unintentional proof of vitamin safety, even in ridiculously high overdosage situations. It is certainly noteworthy that 580 times the normal amount of vitamin D produced, at most, one alleged fatality over a two-year period. Furthermore, there was a total of fewer than two dozen toxicity reports for the entire Boston metropolitan area, after large numbers of people had been ingesting close to a quarter of a million units of vitamin D per liter of milk day after day, month after month, for up to two years. This borders on the extraordinary. Events such as this demonstrate that the margin for error with vitamin D is very large indeed. Though the news reported the vitamin's toxicity, the real story was the vitamin's safety. The scientific literature confirms vitamin D's value.

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