

Vitamin D

Benefits for Bone Health and Beyond

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An internationally recognized expert in the role of vitamin D in health, Dr. Holick serves numerous national committees and editorial boards, has authored more than 260 peer-reviewed publications and 200 review articles, and served on the Institute of Medicine's scientific expert panel for the 1999 Dietary Reference Intakes For Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride.

A Conversation with Dr. Michael F. Holick

Most health professionals know vitamin D for its critical role in increasing the efficiency of dietary calcium absorption and preventing rickets in children. In the past decade, emerging research has also uncovered other important relationships between vitamin D and bone health as well as new information indicating it could potentially play a significant role in strengthening the body's defenses against chronic and autoimmune diseases and in controlling the growth of cells (both normal and cancerous). And while scientific understanding for a potentially much broader role of vitamin D in promoting optimal health has led many experts to call for a several-fold increase in recommended intakes, recent dietary intake studies suggest that many Americans have trouble meeting current recommendations on a consistent basis.

To better understand emerging vitamin D research findings and trends, The Beverage Institute For Health & Wellness (BIHW) of the Coca-Cola Company talked with Michael F. Holick, M.D., Ph.D., Professor of Medicine, Physiology and Biophysics, director of the Vitamin D, Skin and Bone Research Laboratory at Boston University School of Medicine and noted vitamin D researcher.

BIHW: Scientists are engaged in intriguing research to explore potential links between low vitamin D status and increased risk for a number of chronic diseases. Why do investigators think it is worthwhile to explore such a link?

Dr. Holick: In the early 1940s, it was first observed that people living in Vermont, Massachusetts and New Hampshire were more likely to die of cancer — including cancers of the breast, colon and prostate — than people living in southern states such as Texas, South Carolina and Georgia. In the 1990s, it was further demonstrated that living at higher latitudes increased risk not only of deadly cancers, but was also associated with increased risk of type 1 diabetes, multiple sclerosis and hypertension.¹

Although it was intuitive that living at higher latitudes increased the risk of vitamin D deficiency, it took a decade's worth of research to finally uncover the mechanisms by which vitamin D status could impact certain diseases. In brief, we now know that every tissue and cell in the body requires vitamin D for proper function.

Cancer: Vitamin D is one of the most potent hormones for regulating cell growth. Most body cells, including prostate, colon and breast cells, have vitamin D receptors. Some evidence suggests that the active form of vitamin D inhibits the proliferation of cancer cells and induces differentiation into normally functioning cells. Additionally, there are several retrospective and prospective observational studies reporting decreases of 50 percent or more in risk of large bowel cancer and prostate cancer when the levels of 25(OH)D, which is the primary form of vitamin D found in the bloodstream, are greater than 20 ng/mL (50 nmol/L) or when vitamin D intake is increased. Findings are similar for breast cancer.²

Hypertension: Epidemiologists have also known for some time that people living at higher latitudes throughout the world are at higher risk for hypertension, suggesting that adequate vitamin D status from sun exposure might protect against hypertension. To test this hypothesis, hypertensive adults were exposed to a tanning bed that emit-



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Vitamin D: Benefits for Bone Health and Beyond

ted radiation similar to either summer sunlight, which leads to the production of vitamin D₃ in the skin, or winter sunlight, which doesn't lead to vitamin D₃ production, three times a week for three months. The subjects who received the "summer sunlight" radiation had a 180 percent increase in serum 25(OH)D and a decrease of 6 mm Hg in their systolic and diastolic blood pressures, bringing them into the normal range. Serum 25(OH)D and blood pressure didn't change in the subjects who received the radiation that was similar to winter sunlight.²

A possible relationship between adequate vitamin D status and reduced risk for hypertension isn't surprising because 1,25(OH)₂D is one of the most potent hormones for regulating the blood pressure hormone, renin, in the kidneys.² However, we still have a lot to learn in this area.

Heart Disease: It was recently reported that if you are vitamin D deficient, you have more than a 50% higher risk of having your first heart attack. It has also been observed that you reduce your risk of dying of heart disease by as much as 120% when your blood levels of 25(OH)D are > 30 ng/ml.³

Type 1 Diabetes: There is some intriguing new data about adequate vitamin D and some autoimmune diseases. For example, a study involving a special type of nonobese mice that typically develop type 1 diabetes by the 200th day of life found that a daily dose of 1,25(OH)₂D₃ reduced the risk of developing the disease by 80 percent.²

In addition, a 2001 study in Finland that followed a birth cohort of more than 10,000 children found that those who regularly received a supplemental dose of 2,000 IU of vitamin D daily during their first year of life had an 78 percent lower risk for developing type 1 diabetes compared to those who regularly received less than the recommended amount.² These interesting but preliminary findings warrant further investigation.

Type 2 Diabetes: It is now recognized that the insulin producing cells in the pancreas respond to active vitamin D by enhancing insulin production. It was reported that both men and women who ingested 1,200 milligrams of calcium and more than 800 IU of vitamin D per day reduced their risk of developing type 2 diabetes by 33%.⁴

Multiple Sclerosis: Recent observational findings from Harvard's Nurses' Health Study reported that higher intake of vitamin D was associated with a lower risk of developing multiple sclerosis. In addition, in one double-blinded randomized controlled trial, patients with multiple sclerosis received either a vitamin D supplement or a placebo. Results showed that the subjects receiving the vitamin D supplement had increased serum levels of a growth factor associated with the stable phase of multiple sclerosis.² Additional well-designed clinical trials are needed to determine whether vitamin D deficiency increases the risk of multiple sclerosis, or if an increased intake of vitamin D is protective.

BIHW: What are your thoughts about the recent results from the Women's Health Initiative showing that calcium plus vitamin D supplements didn't reduce hip fractures among postmenopausal women?

Dr. Holick: The results aren't really surprising because the subjects received only 400 IU of vitamin D daily, which isn't enough to raise serum 25(OH)D levels into the desirable range. The observation for the Women's Health Initiative showing that calcium and vitamin D supplementation did not reduce hip fractures among post-menopausal women was flawed by the fact that most of the women in the study admitted that at least 60% of the time they did not take their calcium and vitamin D. However, a subset analysis of the women who took their calcium and vitamin D at least 80% of the time showed a statistically significant 29% reduction in risk of hip fracture. Thus, when a post menopausal woman takes an adequate amount of calcium and vitamin D, she is likely to benefit by having a reduction in risk of hip fracture.⁵ Despite some negative studies, most evidence from randomized controlled trials supports a reduction in fracture risk with sufficient vitamin D status, which is given in combination with calcium in most trials. This especially holds true in populations with low vitamin D status and low calcium intakes at baseline.⁶



“Children and adolescents who don't get enough Vitamin D won't obtain this optimal genetically programmed peak bone mass...”

It's also important to know that vitamin D plays a role in supporting muscle function. Several studies indicate that vitamin D inadequacy contributes to muscle weakness and falls in the elderly. We reported that nursing home residents who took 800 IU of vitamin D per day for up to a year reduce their risk of falling by 72%.⁵ It may also be a factor in loss of muscle mass and muscle strength.

BIHW: How does vitamin D affect bone health?

Dr. Holick: Children and adolescents who don't get enough vitamin D won't attain their optimal genetically programmed peak bone mass because they can't sufficiently absorb the dietary calcium needed for the bone mineralization process. In adults, vitamin D deficiency leads to inadequate calcium absorption, which causes secondary hyperparathyroidism. This results in an increased removal of calcium from the bone, leading to bone loss and increased risk of osteoporosis. Vitamin D deficiency also causes a mineralization defect in the skeleton that causes osteomalacia (adult rickets). Unlike osteoporosis, which is char-

acterized by holes in the bone without bone pain, osteomalacia can cause isolated and generalized aches and pains in the bones and muscles. Low serum 25(OH)D levels are associated with muscle weakness in patients with osteomalacia.

BIHW: How much vitamin D do we need each day?

Dr. Holick: In 1997, the Institute of Medicine set Adequate Intakes for vitamin D at 200 IU for ages 1 to 50 years, 400 IU for ages 51 to 70 and 600 IU for ages 71 and over.⁷ However, many in the scientific community now agree that these levels are too low and, assuming no sunlight exposure, many organizations including the National Osteoporosis Foundation recommend an intake of 800 to 1,000 IU of vitamin D₃ daily. This amount helps maximize intestinal calcium absorption and bone health and helps maintain a desirable serum 25(OH)D level of 30 to 100 ng/mL (75 - 250 nmol/L). Although significantly higher than current recommendations, these recommendations are still well within the safe level. It is now recognized that for every 100 IU of vitamin D ingested the blood level of 25(OH)D increases by 1 ng/ml. Thus, in order to raise the blood level of 25(OH)D into the desirable range of 30-100 ng/ml (75-250 nmol/L), children and adults need to ingest 1,000 - 2,000 IU of vitamin D each day to achieve these levels if there is no contribution from sun exposure. We recently conducted a study in healthy adults in Boston at the end of the winter. We gave them 1,000 IU of vitamin D₂ or 1,000 IU of vitamin D₃ per day. The average blood level of the subjects at the end of the winter was approximately 18 ng/ml; 1,000 IU of vitamin D₂ or vitamin D₃ per day raised their blood levels to approximately 28 ng/ml. Thus, to achieve a desirable level of 25(OH)D of > 30 ng/ml, a person needs to ingest at least 1,500 IU of vitamin D per day.⁸ I take a 1,000 IU of vitamin D₃ supplement daily along with a multivitamin that contains 400 IU of vitamin D. My blood level of 25(OH)D is approximately 40 ng/ml.

toxicity only in heavy supplement users who consume more than 10,000 IU daily.

BIHW: Aren't most Americans getting enough vitamin D?

Dr. Holick: No, and that's a problem. We recently estimated vitamin D intakes using 1999-2000 National Health and Nutrition Examination survey data and found that a mere 4 percent of adults 51 and older met or exceeded the current adequate intake (AI) recommendations from food alone. Even when we looked at vitamin D from food plus supplements, this older group, particularly non-Hispanic blacks and Mexican Americans, didn't fare well. However, even among children and teens, the group with the highest intakes, a full 52 percent of non-hispanic black children between the ages of 1 and 8, as well as 31 percent of Mexican-American and 41 percent of non-hispanic white children of that age, failed to meet the AI for vitamin D from food.^{9,10} These intake figures are of concern because, as I've already pointed out, many experts feel the current AI for vitamin D for all ages is set too low for optimal health. As a result, I believe just about anyone can be at risk for vitamin D insufficiency, which we define as a serum 25(OH)D level of less than 30 ng/mL (75 nmol/L).

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Individuals who have reduced ability to produce vitamin D or to utilize body stores of the vitamin need to make an extra effort to ensure they get adequate amounts in their diets and through supplements. For example, dark skin pigmentation and aging greatly reduce the skin's capacity to produce vitamin D₃ from sunlight exposure. At latitudes above 35°N and below 35°S, there's not enough sunlight during the winter months to induce the skin to produce vitamin D₃, which in the U.S. means those living north of San Francisco, California; Springfield, Missouri, Richmond, Virginia and Atlanta, Georgia. In the obese, vitamin D₃ stores are sequestered deep inside body fat, which makes it less available. Thus, most obese patients are vitamin D-deficient and need twice as much vitamin D to be vitamin D sufficient.

BIHW: What factors are contributing to low dietary intakes of vitamin D?

Dr. Holick: For one thing, few foods except cod liver oil and oily fish such as salmon, mackerel, tuna, and herring contain significant amounts of vitamin D naturally. Another factor is that while fortified foods are the major dietary sources of vitamin D in the U.S., only a few types of foods are fortified. For example, fluid milk has been fortified with vitamin D since the 1930s, but dairy products like cheese, yogurt and ice cream have generally not been fortified. This has made getting enough vitamin D particularly challenging for those who avoid milk due to lactose intolerance.

SOURCES OF VITAMIN D	
SOURCE	VITAMIN D CONTENT
Exposure to sunlight (5-10 minutes)	~3,000 IU of vitamin D ₃
SALMON	
Fresh, farmed (3.5 oz)	100-250 IU of vitamin D ₃ or D ₂
Canned (3.5 oz)	300-600 IU of vitamin D ₃
FORTIFIED FOODS	
Fortified Milk (1 cup)	~100 IU of vitamin D ₃
Fortified orange juice (1 cup)	~100 IU of vitamin D ₃
Fortified breakfast cereal (1 serving)	~100 IU of vitamin D ₃
Source: U.S. Department of Agriculture, Agricultural Research Service. 2005. USDA National Nutrient Database for Standard Reference, Release 18. Nutrient Data Laboratory Home Page. Accessed May 19, 2006.	

The Tolerable Upper Intake Level for vitamin D is currently set at 2,000 IU for ages 1 and older. Clinically we tend to see vitamin D

BIHW: *Are any new measures being taken to improve vitamin D intake in the U.S.?*

Dr. Holick: Yes. In 2003, the U.S. Food and Drug Administration approved the addition of vitamin D to calcium-fortified juices and juice drinks at 100 IU per eight fluid ounce serving, or 25% the current Daily Value (DV), which is similar to the level set for milk. Some breakfast cereals and some brands of yogurt and cheese are also now fortified with vitamin D.

In addition, the USDA has also begun a project to reanalyze vitamin D content in the U.S. food supply using advanced methodologies. This is key to helping us better understand how much vitamin D people are consuming and how consumption levels relate to health.

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BIHW: *What should people look for when choosing fortified foods and supplements?*

Dr. Holick: Although there have been some studies using very high doses of vitamin D2 and vitamin D3 that suggested that vitamin D2 was less effective than vitamin D3 in maintaining serum 25(OH)D levels, we recently observed that in healthy adults ingesting 1,000 IU of vitamin D2 or 1,000 IU of vitamin D3 either in pill form or in orange juice was equally effective in maintaining blood levels of 25(OH)D. Thus, with this new information, it appears that vitamin D2 is equally as effective as vitamin D3 in maintaining 25(OH)D levels.⁸

Vitamin D3 is derived from animal sources and is also the form synthesized by skin with sunlight exposure. Vitamin D2 is derived from plant and yeast sources.

BIHW: *How can health professionals help ensure people get enough vitamin D?*

Dr. Holick: We need to educate people about why it's important to meet vitamin D recommendations and how. Make sure they understand that getting enough vitamin D-fortified milk, orange juice, cereals and/or supplements should be a dietary priority.

I'd also like to see routine evaluation of serum 25(OH)D levels for all children and adults, and especially for those in at-risk groups such as African Americans, the elderly and people with osteoporosis, as well as those who faithfully use sunscreen routinely or live in northern climates.

The views and opinions expressed by the experts and organizations quoted in this article are their own and do not necessarily represent the views of any institution or association to which they belong, nor The Beverage Institute For Health & Wellness or any member of the Beverage Institute Advisory Council.

Additional Resources

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