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REPORT

A New Light on Vitamin D

Vitamins are a crucial part of maintaining biological stability. Yet, it has only been within the past few years that researchers and physicians alike have realized their potential not only to respond to deficiency, but to promote better general health.1 One of the most essential-yet oddly often overlooked- nutrients is vitamin D.

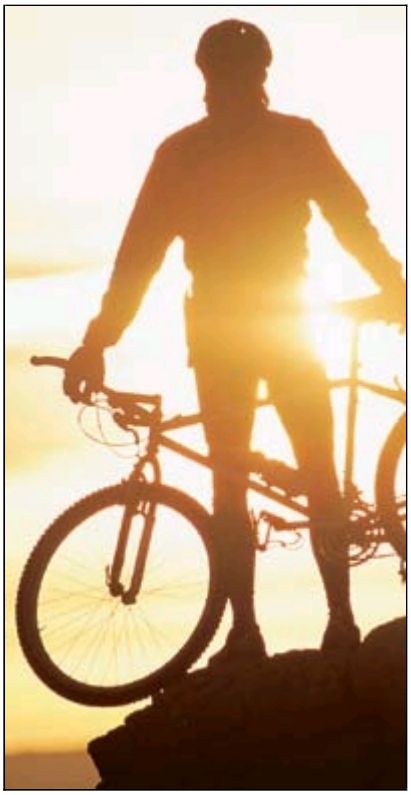
Although written accounts of diseases such as rickets and osteoporosis date back centuries, it wasn't until 1919 that researchers first began to realize how important vitamin D was to the prevention and correction of bone disorders.2 Since then, research into this important nutrient has concluded that not only is it more than a simple vitamin-actually functioning as a hormone-but that it also plays a significant role in bone formation, the promotion of nerve function and may even help prevent certain forms of cancer.

While today the word vitamin is a household word, it wasn't until the early 20th century that it first began making its rounds in the common vernacular. First appearing in dictionaries in 1912, the term vitamin was originally coined to describe the organic substances in food that are essential for most of the biochemical processes in the body.3

Since then, scientists have identified 13 vitamins that are considered essential for good health-essential because they are required for life and because the body does not manufacture these nutrients itself. In other words, they must be obtained from external sources, such as food or supplements. These "essential vitamins" are divided into two groups, fat soluble (stored in the fat cells) and water soluble (used and excreted through urine). Fat-soluble vitamins include A, D, E and K. The water-soluble essential vitamins are C (ascorbic acid), B1 (thiamin), B2 (riboflavin), B3 (niacin), B5 (pantothenic acid), B6 (pyridoxine), B12, folic acid and biotin.4

What is vitamin D?

Most people think of bones as static, rigid, unchanging structures that form the internal framework of their bodies. In reality, however, bones are dynamic living tissue composed of a variety of cell types that co-exist in a constant battle between two conflicting processes-formation and resorption. Through these two actions, bone is continually remodeled to maintain stability and preserve proper functioning. To achieve this, our bodies require a sufficient and reliable supply of vital minerals-most notably calcium and phosphorus-and a mechanism to efficiently absorb them. Enter vitamin D.



Even though it's not one of the most talked-about vitamins, vitamin D's importance to maintaining health cannot be overstated. Years of painstaking research has proven conclusively that vitamin D is necessary for both the efficient absorption of dietary calcium and phosphate, as well as their metabolism once ingested.5 In addition, vitamin D has been implicated in playing an important role in a wide variety of actions elsewhere in our physiology-everything from improving immune function and blood cell formation to fostering normal muscle contractions, stimulating neural growth and regulating cardiac action.6

Sources of vitamin D

Although vitamin D enters our bodies through a variety a different mechanisms, such as diet and nutritional supplementation, the primary resource is via exposure to sunlight. Research has shown that when exposed to the sun's ultraviolet light (UVB), a cholesterol compound in the skin is transformed into a precursor of vitamin D (called vitamin D3) which then enters into our circulation.7 As a result, most of our physiological requirements for vitamin D are actually provided for by casual exposure to sunlight. In fact, researchers have estimated that as much as 80% to 100% of an individual's daily requirement for vitamin D comes from simple exposure to sunlight.8

DAILY VITAMIN D REQUIREMENTS*

LIFE-STAGE	MEN	WOMEN
Ages 19-50	5 mcg or 200 IU	5 mcg or 200 IU
Ages 51-69	10 mcg* or 400 IU	10 mcg* or 400 IU
Ages 70+	15 mcg or 600 IU	15 mcg or 600 IU

*1 mcg vitamin D = 40 International Units (IU)
*According to the National Institute of Health

Our secondary source of vitamin D is dietary. While some foods have a small amount of vitamin D naturally (egg yolks, fatty fish such as salmon and fatty fish oils including cod liver oil) fortified foods, such as milk, typically offer the highest level of dietary vitamin D, about 100 IU or 25% of the daily requirements.9

How does vitamin D work?

While researchers still strive to uncover all of the mysteries surrounding the mechanism behind vitamin D's control over mineral metabolism, there are three primary target tissues for its biological actions: intestine, bone and kidney.

The small intestine is an integral part of the human body's ability to stimulate both the absorption and active transport of dietary calcium. Research has shown that in the small intestine, up to 90% of the calcium absorption is vitamin D-dependent.10 Furthermore, according to studies performed at the University of Pennsylvania's School of Medicine, the proximal duodenum holds the greatest concentration of vitamin D receptors in the body. These receptors, once joined with ingested vitamin D, facilitate increased serum calcium levels that are used throughout the body. Without this potent role contributed by vitamin D, calcium serum levels would be seriously compromised.11

In the case of bone, the principal actions of mineral metabolism are a byproduct of vitamin D's effect on the intestine. Because the action of the intestine increases biophysical calcium absorption, increased availability of minerals for incorporation into bone is derived from vitamin D. When there is inadequate calcium in the diet to satisfy the body's calcium requirement, vitamin D communicates to the osteoblasts (bone producing cells) that signal osteoclast (bone resorbing cell) precursors to mature and dissolve the calcium stored in the bone. As such, vitamin D plays a key role in regulating the proliferation and differentiation of both types of bone remodeling cells-those responsible for bone breakdown and those responsible for bone reformation.8

The kidneys represent the third prominent tissue affected by vitamin D. According to researchers at the Boston University Medical Center once vitamin D is in circulation, it is metabolized in part by the kidney to become 1,25-dihydroxyvitamin D, the receptors for which are found 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 and gonads. In addition, the kidneys function to enhance re-absorption of calcium and other minerals from the renal fluid. As bones are being remodeled on a continual basis, there is a constant release or mobilization of calcium stores from these sites-and the kidneys aid in retaining the minerals for recycling back to bone.12

Factors influencing vitamin D Levels

While there are many factors that affect the level of vitamin D in the blood, most relate to the cutaneous synthesis of vitamin D3. Location, time of day, season, skin pigmentation, use of sunscreen, age and dietary intake all play an important role in the circulating level of vitamin D.13

Location, for example can dramatically affect the production of vitamin D3 in the skin. Researchers have found that individuals living in higher latitudes, such as Boston, Massachusetts (42o N latitude) produce little or no vitamin D from November to February, while 10o farther north in Edmonton, Canada, this period is extended from October to March.14 To maintain minimal levels of vitamin D during these months, reserves of vitamin D produced in the summer and stored in the fat cells become liberated from their reservoirs. However, researchers in Canada have recently shown that during winter months at least 34% of the northern population are vitamin D deficient despite the reserves and require supplementation.15

Reducing the skin's UVB exposure via sunscreen or clothing can cause similar vitamin insufficiencies since they retard the skin's ability to absorb radiation.16 According to a recent study of veiled women in Turkey, for example, out of 51 women examined (ages 14 to 63), 82% were found to be severely vitamin D deficient, while another 8% were moderately deficient. In addition, about half of the deficient women complained of muscle pain, weakness or fatigue-symptoms consistent with profound vitamin deficiency. These results confirm that reduced exposure to sunlight compromises the endogenous levels of vitamin D.17

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The impact of vitamin D deficiency

Because of vitamin D's far-reaching biochemical impact, the consequences of even a slight deficiency can be quite serious-resulting in everything from gross abnormalities in bone metabolism to hyperparathyroidism and an increased risk of developing Type I diabetes.

As the body depletes its stores of vitamin D, intestinal calcium absorption decreases from approximately 40% to no more than 15%.18 This results in a cascade of physiological events. The lowered serum calcium concentration stimulates the production of parathyroid hormone (secondary hyperparathyroidism) which then stimulates the bone resorbing cells to increase their activity to bring the serum concentrations of calcium back up to normal. Since adequate calcium is no longer available for mineralization of new bone, substantial bone loss may result. This culminates in chronic pain, increased risk of both vertebral and nonvertebral fractures, and concomitant morbidity.19

Who may need extra vitamin D to prevent a deficiency?

The conditions that increase the risk for developing vitamin D related health problems are relatively common. Menopause, old age, lack of sun and improper diet all contribute to vitamin deficiencies. Evidence suggests, for example, that the skin's ability to convert vitamin D to its active form decreases with age.20 Research has shown that by the time we are 65 years-old, changes to the structure of the skin reduce production of vitamin D by up to 60%.21 Because of this decreased ability to form vitamin D, the circulating levels of vitamin D substantially increases the risk of developing osteopenia-reduced bone mass.22

Persons with kidney disorders, either related to trauma or simply to aging are also prime candidates for vitamin D supplementation. According to researchers at Northwestern University, a variety of bone diseases, such as osteitis fibrosa develops relatively early in cases of chronic renal failure. In such cases where the kidneys are unable to convert vitamin D to its active form, supplementation with vitamin D3 is encouraged.23

Too much of a good thing

While it's clear that vitamin D is essential for good health, it is equally important to realize that moderation is still key. Since it is stored in the fat cells, over-consumption may result in vitamin D toxicity. While rarely lethal, vitamin D toxicity can cause a host of painful problems, including nausea, vomiting, constipation, weakness and weight loss. It is also associated with elevated levels of blood calcium, which can cause cognitive problems and heart arrhythmia.24

Vitamin D toxicity induced through sun exposure or diet alone is not likely. It is much more likely to occur from high intakes of vitamin D in supplements. Published cases involving vitamin D toxicity all involve an intake in excess of 40,000 IU/day, or roughly 100 times the recommended level.25

CURRENT RESEARCH AND VITAMIN D

Alzheimer's disease

Although research into the role of vitamin D in the human brain is still in its infancy, results to date have suggested its possible use in the treatment of neurodegenerative disorders.

Several years ago, researchers in North Carolina performed a study to examine the role of vitamin D in cognitive ability. In that study, radio-labeled vitamin D was injected into rodents to trace the areas of the brain affected by the nutrient. Their results showed that several key areas of the brain involved in both memory and cognitive processes have receptors for vitamin D. In addition, since these same areas are those affected by age-dependent neural disorders, vitamin D supplementation may have a role in combating neurodegenerative diseases.26

To further examine the possible benefits of vitamin D to diseased neural tissue, a group working in Pennsylvania recently studied the effect of vitamin D on neural tissue growth. In their study, adult rat brain tissue was treated with 1,25-dihydroxyvitamin D3, the metabolized product of vitamin D-via a single intracerebroventricular injection. The results showed that vitamin D elicited a two-fold increase in nerve growth factor mRNA in both the hippocampus and cortex, suggesting a possible role in the treatment of neurodegenerative disorders such as Alzheimer's disease.27

Treating cancer

Vitamin D has long been suspected of being a natural chemopreventative agent. Years of research now suggest that vitamin D may actively protect against several forms of cancer by inhibiting cancer cell growth, causing apoptosis, and even by inducing cellular re-differentiation-the conversion of cancers cells back to normal cells.

To further understand its role in cancer prevention, researchers in Italy performed a study to determine the effects of vitamin D on prostate cancer cells. In that study, vitamin D3 was introduced to several human prostate cancer cells that had been treated with KGF-one of the intraprostatic growth factors that are suspected in participating in the progression of prostate cancer. The results showed that vitamin D3 dose-dependently decreased basal and KGF-induced prostate cancer cell growth, and induced cancer cell apoptosis. These results strongly suggest that vitamin D3 is a potential chemodestructive agent.28

In another provocative cancer study, researchers at the Harvard School of Public health reviewed the effects of dietary calcium and vitamin D on 88,691 women over 16 years to determine the relationship to breast cancer. Of that sample, 3,482 women (premenopausal = 827, postmenopausal = 2,345, and uncertain menopausal status = 310) were identified as having invasive breast cancer. These findings indicated that dietary intake of vitamin D was not significantly associated with breast cancer risk in postmenopausal women. In premenopausal women, however, daily high intake of low-fat dairy products (500 IU/day) was associated with a reduced risk of breast cancer. These results suggest that at increased levels vitamin D may minimize the risk of premenopausal women for developing breast cancer.29

Treating and preventing osteoporosis

Osteoporosis is a painful, disabling and disfiguring health deficit that is entirely preventable given early detection and the reversal of the causes-one of which is a deficiency of vitamin D.30 Sometimes called "the silent disease," because of its sinister ability to progress for years undetected, osteoporosis is a metabolic bone disease characterized by serious loss of bone mass or disintegration of the bone architecture that results in increased risk of bone fractures.

Owing to the relationship between vitamin D and mineral metabolism, scientists have concluded that increased levels of vitamin D effectively reduce the risk of osteoporosis and related fractures. Researchers at Harvard have recently finished an 18-year prospective analysis of the level of vitamin D in 72,337 postmenopausal women and found that women with a high daily intake of vitamin D (>12.5 micro g vitamin D/d) through food and supplements had a 37% lower risk of hip fracture. These researchers further concluded that neither milk nor a high-calcium diet appears to reduce fracture risk and suggest that vitamin D supplements may be a prudent method for maintaining adequate levels of vitamin D.31

Although more commonly associated with women, osteoporosis affects more than five million men in the United States with significant morbidity and mortality. In a recent article published in the Journal of Gender Specific Medicine, researchers point out the need for preventative measures, such as maintaining adequate levels of circulating vitamin D. Furthermore, daily vitamin D supplements are also suggested to treat and reduce the risk factors associated with the disease.32

Looking ahead

Despite all that we have learned about the value of essential nutrients like vitamin D, science has uncovered but a mere fraction of their enormous potential. Researchers continue to explore and further define their role in the human body, hoping to understand the delicate biochemical interactions and their impact on health.

References

1. Swain R, et al. Vitamins as therapy in the 1990s. J Am Board Fam Pract 1995 May-Jun;8(3):206-16.

2. Pedersen S. Vitamin D: Maximizing the most of minerals. 2000;1: 4-5.

3. Pedersen S. Vitamin D: Maximizing the most of minerals. 2000;1: 6-7.

4. Goldberg, B. Alternative Therapies. 2002; 393-398.

5. Atkins, R. Dr. Atkins' Vita-Nutrient Solution. 1998; 104.

6. Gulati S, et al. Hypocalcemic heart failure masquerading as dilated cardiomyopathy. Indian J Pediatr 2001 Mar;68(3):287-90.

7. Lehmann B, et al. UVB-induced conversion of 7-dehydrocholesterol to 1alpha,25-dihydroxyvitamin D3 in an in vitro human skin equivalent model. J Invest Dermatol 2001 Nov;117(5):1179-85.

8. Holick MF. Vitamin D: A millenium perspective. J Cell Biochem 2003;88(2):296-307.

9. Goldberg, B. Alternative Therapies. 2002; 393-398.

10. Bronner F. Mechanisms of intestinal calcium absorption. J Cell Biochem 2003;88(2):387-93.

11. Pazianas M et al. Efferent loop small intestinal vitamin D receptor concentration and bone mineral density after billroth II (Polya) gastrectomy in humans. Calcif Tissue Int 2003 Feb 10.

12. Fukugawa M et al. Calcium homeostasis and imbalance. Nephron 2002;92 Suppl 1:41-5.

13. Pfeifer M et al. Vitamin D and muscle function. Osteoporos Int 2002 Mar;13(3):187-94.

14. Webb AR, et al. Influence of season and latitude on the cutaneous synthesis of vitamin D3: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D3 synthesis in human skin. J Clin Endocrinol Metab 1988 Aug;67(2):373-8.

15. Rucker D, et al. Vitamin D insufficiency in a population of healthy western Canadians. CMAJ 2002 Jun 11;166(12):1517-24.

16. Simon J, et al. Fractures in the elderly and vitamin d. J Nutr Health Aging 2002;6(6):406-12.

17. Grootjans-Geerts et al. A pilot study of hypovitaminosis D in apparently healthy, veiled, Turkish women: severe vitamin D deficiency in 82%. Ned Tijdschr Geneeskd 2002 Jun 8;146(23):1100-1.

18. Holick MF. The cutaneous photosynthesis of previtamin D3: a unique photoendocrine system. J Invest Dermatol 1981 Jul;77 (1):51-8.

19. Al Faraj S, et al. Vitamin D deficiency and chronic low back pain in Saudi Arabia. Spine 2003 Jan 15;28(2):177-9.

20. Wemeau JL. Calciotropic hormones and ageing. Horm Res 1995;43(1-3):76-9.

21. Cerimele D et al. Physiological changes in ageing skin. Br J Dermatol 1990 Apr;122 Suppl 35:13-20.

22. Morley JE, et al. Nutrition in the elderly. Ann Intern Med 1988 Dec 1;109(11):890-904.

23. Ho LT, et al. Renal osteodystrophy in chronic renal failure. Semin Nephrol 2002 Nov;22(6):488-93.

24. Atkins, R. Dr. Atkins' Vita-Nutrient Solution. 1998; 106.

25. Vieth R. Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety. Am J Clin Nutr 1999 May;69(5):842-56.

26. Musiol IM et al. Vitamin D nuclear binding to neurons of the septal, substriatal and amygdaloid area in the Siberian hamster (Phodopus sungorus) brain. Neuroscience 1992 Jun;48(4):841-8.

27. Saporito MS, et al. Pharmacological induction of nerve growth factor mRNA in adult rat brain. Exp Neurol 1993 Oct;123(2):295-302.

28. Crescioli C, et al. Vitamin D3 analogue inhibits keratinocyte growth factor signaling and induces apoptosis in human prostate cancer cells. Prostate 2002 Jan 1;50(1):15-26.

29. Shin MH, et al. Intake of dairy products, calcium, and vitamin d and risk of breast cancer. J Natl Cancer Inst 2002 Sep 4;94 (17):1301-11.

30. Love C. Dietary needs for bone health and the prevention of osteoporosis. Br J Nurs 2003 Jan 9-22;12(1):12-21.

31. Feskanich D, et al. Calcium, vitamin D, milk consumption, and hip fractures: a prospective study among postmenopausal women. Am J Clin Nutr 2003 Feb;77(2):504-11.

32. Epperly TD, et al. Diagnosis, prevention, and treatment of osteoporosis in men. J Gend Specif Med 2002 Nov-Dec;5(6):33-8.

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