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REPORT

Guarding Against the Dangers of Vitamin D Deficiency

By Tiesha D. Johnson, BSN, RN



The long, dark days of another winter have come and gone. Tens of millions of Americans would be surprised to learn that winter has left them deficient in vitamin D. Your chances of being one of them are probably much greater than you imagine.

Vitamin D is synthesized in the skin in response to sunlight exposure, but few people achieve optimal levels this way, in part due to the limited ultraviolet light available during the winter months. This seasonal deficit is compounded by the fact that many people avoid sun exposure during the spring and summer months because of concern about premature skin aging and cancers like melanoma. Alarming new research suggests that these factors are contributing to a year-round epidemic of vitamin D deficiency, particularly in elderly adults.

Vitamin D does far more than promote healthy teeth and bones. Its role in supporting immunity, modulating inflammation, and preventing cancer make the consequences of vitamin D deficiency potentially devastating. A growing number of scientists who study vitamin D levels in human populations now recommend annual blood tests to check vitamin D status.

In this article, we examine the factors that contribute to the widespread prevalence of vitamin D deficiency, the latest studies supporting vitamin D's critical role in preventing disease, and how much supplemental vitamin D you need to achieve optimal blood levels.

VITAMIN D DEFICIENCY: AN OVERLOOKED EPIDEMIC

Vitamin D is a fat-soluble prohormone—that is, it has no hormone activity itself, but is converted to a molecule that does, through a tightly regulated synthesis mechanism. Its two major forms are vitamin D₂ (or ergocalciferol) and vitamin D₃ (or cholecalciferol). Vitamin D also refers to metabolites and other analogues of these substances. Vitamin D₃ is produced in skin exposed to sunlight, specifically ultraviolet B radiation.

While vitamin D is best known for promoting calcium absorption and bone health, researchers have recently discovered important new roles for this versatile vitamin.¹ As an active hormone,² vitamin D is now seen as playing a central role in controlling immunity and inflammation,^{1,3,4} two vital processes that are tied to a host of age-related disease conditions.⁵⁻¹⁰

Just as scientists are discovering critical new roles for vitamin D, they are also finding that shockingly few people have blood levels of vitamin D adequate to support their daily needs.^{5,6} One leading researcher has referred to this deficit as a “vitamin D epidemic.”⁷ Estimates of the percentage of US adolescents and adults who are vitamin D deficient range from 21% to 58%,¹¹ while as many as 54% of homebound older adults are believed to be vitamin D deficient.¹²

Because vitamin D₃ is obtained in humans primarily as a result of exposure to sunlight,⁸ this puts people living outside the tropics at particular risk for vitamin D deficiency, especially from late fall to early spring.⁹ Further compounding the problem, many public health officials are concerned that their warnings about avoiding the sun because of skin cancer risk may in fact be causing people to limit their sun exposure to an unhealthy extent.^{10,13}

Because sun exposure does pose significant health risks, and most Americans live outside of the regions where they can get adequate sun in winter, perhaps the best way to address this dilemma is by paying close attention to your blood levels of vitamin D and optimizing them through appropriate supplementation. Life Extension recommends that adults check their blood levels and supplement with enough vitamin D₃ to achieve optimal blood levels.⁶⁻⁸

To meet all of the body's needs for proper vitamin D activity, many scientists now advocate supplementing with doses that are considerably higher than the minimums currently recommended by the Institute of Medicine.¹⁴ While vitamin D can be obtained

through a few dietary sources such as fish, eggs, and dairy products, these foods fail to provide the daily levels required by most individuals, thus necessitating vitamin D supplementation.

HOW VITAMIN D CONTROLS CELL FUNCTIONS

Vitamin D's applications in promoting optimal health stem from its ability to control production of vital proteins by switching genes on and off, and thus helping to determine the fate of cells. Cells affected by the active form of vitamin D, known as calcitriol,¹⁵⁻¹⁷ stop growing and reproducing, and rapidly mature into their final forms.^{3,4,17,18}

These effects help prevent the proliferation (uncontrolled growth) of potentially cancerous cells,¹⁹⁻²⁴ while stimulating cells to differentiate (mature) so that they can carry out their mature functions, such as stimulating immune system activity.^{3,4,25-27}

Since uncontrolled reproduction of immature cells is the defining feature of cancers, vitamin D may have important cancer-preventive effects. Because of its unique ability to switch cell functions on and off, vitamin D has a dual effect that can modulate immune function³ by both boosting deficient immune function and quieting overactive autoimmunity.²⁸

Vitamin D may further help to reduce the excessive inflammation and oxidative damage implicated in conditions such as osteoarthritis,^{29,30} chronic obstructive pulmonary disease (such as emphysema),³¹⁻³³ cardiovascular disease,^{34,35} and metabolic syndrome.^{36,37} Low vitamin D levels are linked to increased risk for all these conditions,³⁸⁻⁴⁶ highlighting the importance of regular vitamin D blood tests to detect and correct deficiencies before they contribute to the onset of disease.

APPLICATIONS FOR PREVENTING AND TREATING CANCER

Strong epidemiological data now implicate low vitamin D levels in at least 16 different malignancies.⁴⁷ Powerful clinical evidence indicates that vitamin D may be useful in preventing and even treating colon and prostate cancers, while suggestive evidence points to its effects in countering lung, breast, skin, and other cancers.^{16,47}

COLON CANCER

Twenty-five years of research suggests that detecting and correcting vitamin D deficiency may be especially important in averting colon cancer, a disease that claims approximately 56,000 lives each year in the United States.⁴⁸

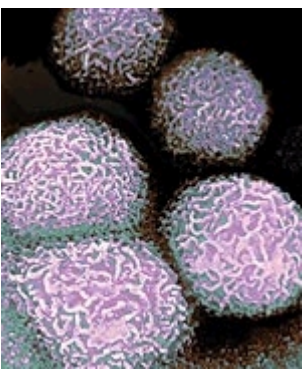
An early study of 1,954 men found that those with the lowest vitamin D intake had more than double the risk of colon cancer compared to men with the highest intake.⁴⁹ Colon cells reproduce very quickly, placing them at risk for becoming malignant. When active vitamin D was applied to colon cells in culture, reproduction rates fell by 57% in normal colon tissue and by 52% in patients with familial adenomatous polyposis, an inherited syndrome characterized by many pre-cancerous polyps.⁵⁰ In a laboratory study, pretreatment with vitamin D made colon cancer cells easier to kill with hydrogen peroxide and other natural oxidants present in the bowel.⁵¹



A large randomized trial from 2003 helped to establish a clinical role for vitamin D in preventing colon cancer.⁵² Eight hundred three subjects with previous colorectal adenomas (which can lead to cancer if they recur) were given calcium supplements or placebo, and their rates of adenoma recurrence were measured. Calcium supplements reduced the risk of adenoma recurrence by 29% in subjects with normal D levels. This study demonstrated that both calcium and adequate vitamin D levels are needed to reduce colon cancer risk.

In a 2006 study,⁵³ researchers surgically divided individual adenomatous (potentially precancerous) polyps, removing approximately 50% from 19 patients. They marked the remnants of the polyps in the intestine so they could identify them later, and studied cell proliferation in the polyp tissue before and after six months of treatment with oral vitamin D3 (400 IU) and calcium carbonate (1500 mg, three times daily) or placebo. Adenomas from patients treated with calcium and vitamin D3 showed marked declines in cell proliferation and other signs of cancerous change, while there was no change in tissue taken from the control patients.

Cancer prevention specialists at the University of California recently conducted an extensive review of scientific papers published worldwide between 1966 and 2004. Their analysis suggested that taking 1000 international units (IU) of vitamin D3 daily lowers an individual's risk of developing colorectal cancer by 50%. The researchers recommended increased intake of vitamin D3 as an inexpensive, non-toxic preventive therapy for colon cancer. Specifically, they hope to see the federal government officially recommend intake of 1000 IU per day of vitamin D3 for cancer prevention.⁴⁸



Scanning electron micrograph of human colon carcinoma.

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PROSTATE CANCER

Optimal levels of vitamin D may also help protect prostate health.^{19,54}

Aware that low vitamin D levels are a major risk factor for prostate cancer,^{40,55,56} researchers examined the vitamin's preventive effect in a cancer-prone mutant strain of mice.⁵⁷ Mutant and control mice were given vitamin D for four months either before or after developing the first signs of cancer. Vitamin D substantially reduced the occurrence of early cancerous changes in tissue, yet appeared to have no effect on the androgen (male hormone) system. This is crucial, because many conventional prostate cancer drugs impair androgen function. Human prostate cancer cells in culture show similar reductions in cancerous changes and proliferation when treated with vitamin D3 and a synthetic retinoid (a vitamin A-like compound).⁵⁸

A 1998 study demonstrated that vitamin D can reduce prostate cancer growth in human subjects. Seven men with recurrent prostate cancer following surgery or radiation (as measured by increasing levels of prostate-specific antigen, or PSA) were given a prescription form of vitamin D called calcitriol (Rocaltrol®) at increasing doses from 0.5 to 2.5 mcg (20-100 IU) per day. The rate of PSA increase (an indicator of disease progression) during treatment fell significantly compared to the rate before treatment in six of the subjects, suggesting a slowing of prostate cancer progression.⁵⁹ In a related study, weekly dosing with calcitriol (at 20 IU per kilogram of body weight) increased median PSA doubling time in men who had been treated for prostate cancer.^{60,61} An increased PSA doubling time means that it takes longer for the PSA cancer marker to elevate (double), which is a favorable sign.

Treatment of existing prostate cancers with vitamin D also shows promise. In a 2006 Phase II clinical trial,⁶² researchers administered calcitriol three times weekly (at up to 12 mcg [480 IU] per dose) with the potent steroid dexamethasone. Thirty-seven men with androgen-independent prostate cancer were treated for at least one month. Eight patients had notable decreases in levels of PSA, a marker for tumor size. The researchers concluded that because there was minimal toxicity from this combination, it is a safe and feasible anti-tumor treatment.

VITAMIN D: WHAT YOU NEED TO KNOW

- Low dietary intake and limited sun exposure have led to an epidemic of vitamin D deficiency. Health experts now advise adults to regularly check their blood levels of vitamin D and to address deficiencies with supplemental vitamin D.
- Vitamin D plays many essential roles throughout the body—enhancing calcium absorption, contributing to healthy bone mass, supporting immune function, quelling inflammation, and helping to fight cancer.
- Clinical studies support vitamin D's role in preventing and treating colon and prostate cancers, and emerging studies suggest vitamin D may help avert cancers of the breast, ovaries, head, and neck, among others.
- Vitamin D quells inflammation that may exacerbate chronic heart failure, and in combination with other nutrients, benefits people with chronic heart failure. Vitamin D also shows promise in preventing both type I and type II diabetes, and offers important support for immune health. Vitamin D may help prevent wound infections and flu, support the body's defense against tuberculosis, and boost immune function in patients with kidney failure.
- Vitamin D likewise may help to alleviate seasonal affective disorder (SAD), a type of depression experienced during the winter months due to decreased sunlight.



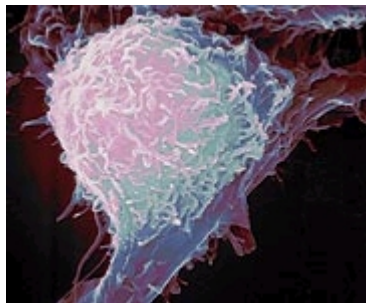
BREAST AND OTHER CANCERS

Abundant laboratory research demonstrates that vitamin D prevents human breast cancer cell proliferation and enhances the differentiation of cells into normal, healthy tissue.^{18,21-23,63,64} Powerful evidence also indicates that rates of breast cancer, like those of many other cancers, are lower in populations with greater exposure to sunlight or greater dietary intake of vitamin D.⁶⁵⁻⁶⁷

Similarly, enticing (though not yet clinically proven) evidence suggests a role for vitamin D supplementation in preventing or treating other cancers, including ovarian cancer, non-Hodgkin's lymphoma, and cancers of the head and neck.^{20,47,68-70} Many cancer specialists advise checking vitamin D levels at least once a year, and supplementing with vitamin D if a deficiency is detected.^{6,40}

VITAMIN D HELPS ALLEVIATE HEART FAILURE

Heart failure—the heart's inability to pump enough blood to meet the body's requirements—is a leading cause of death in industrialized nations.⁷¹ Scientists believe that elevated levels of circulating pro-inflammatory cytokines may contribute to heart failure, and that vitamin D may offer heart-protective benefits by quelling these inflammatory mediators.⁷²



Scanning electron micrograph of prostatic cancer cell.

In a recent double-blind clinical trial, 123 patients with congestive heart failure were randomly assigned to receive either vitamin D3 (50 mcg [2000 IU] per day) plus 500 mg of calcium or placebo plus 500 mg of calcium.⁷² Over the nine months of the study, patients who supplemented with vitamin D had greatly increased levels of the anti-inflammatory cytokine interleukin-10 and lower levels of the pro-inflammatory cytokine tumor necrosis factor-alpha. Scientists believe that by reducing the inflammatory environment in congestive heart failure patients, vitamin D3 holds promise as an anti-inflammatory therapeutic for people suffering from heart failure.

A 2005 study reported on the use of vitamin D and other nutrients in chronic heart failure.⁷¹ In a randomized trial, 28 chronic heart failure patients supplemented with 200 IU of vitamin D, 150 mg of coenzyme Q10, minerals, antioxidants, and B vitamins or placebo for nine months. The supplemented patients had an impressive 17% decrease in the heart's left ventricular volume, which typically is increased in chronic heart failure and adds to the work required of the already-fatigued heart muscle. By contrast, left ventricular volume increased 10% in the placebo group. Supplemented patients also had a modest increase in quality-of-life scores. These findings indicate that vitamin D supplementation, in combination with coenzyme Q10, vitamins, and minerals, can offer important support for people with chronic heart failure.

ENSURING OPTIMAL VITAMIN D LEVELS

Health experts urge all adults to have regular (at least annual) checks of vitamin D levels in their blood.⁷ There is a good chance that you will be deficient for at least part of the year if you live in North America, according to those experts.^{6,55} Once a deficiency is identified, supplementation can safely restore levels to the normal range. Checking vitamin D status again after a few months of supplementation is also advised.

While the federal government's recommended dietary allowance (RDA) of vitamin D is 400 IU (10 mcg) daily,⁸³ many health experts now advise daily doses of at least 800 IU (20 mcg) of vitamin D.⁸⁴ Life Extension recommends that healthy adults supplement each day with at least 1000 IU of vitamin D. Elderly adults may benefit from higher doses such as 2000 IU daily, and even up to 5000 IU daily. Research published over the last decade suggests that vitamin D toxicity is unlikely at daily intake levels of less than 10,000 IU (250 mcg).^{14,85-88}

Comprehensive research reviews conducted by a leading authority on vitamin D, Dr. Michael Holick, suggest that a healthy serum level of vitamin D (25-hydroxyvitamin D) is 75-125 nmol/L. Serum levels within this range have been associated with improved bone health and muscle strength, as well as protection against numerous cancers.^{6,7,89}

As with many supplements, an appropriate dosage is critical for efficacy and safety. Long-term supplementation with very high doses of vitamin D can cause dangerous elevations in blood calcium levels.^{90,91} Too much calcium in the blood can rapidly cause poor muscle and nerve function,⁹² and long-term elevations increase the risk of kidney stones.⁹³ Anyone taking extremely high doses of vitamin D should be monitored for signs and symptoms of vitamin D toxicity, which include nausea, vomiting, poor appetite, constipation, weakness, heart arrhythmias, kidney stones, and elevated blood levels of cholesterol, calcium, or liver enzymes.^{83,84} Vitamin D is contraindicated in individuals with hypercalcemia (high blood calcium levels).^{83,84} People with kidney disease and those who use digoxin or other cardiac glycoside drugs should consult a physician before using supplemental vitamin D.^{83,84}

Life Extension recommends that all adults check their blood vitamin D levels at least once a year. If levels are low, discuss supplementation with your health care provider, and then follow up with repeat testing after a few months.

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VITAMIN D MAY HELP PREVENT DIABETES

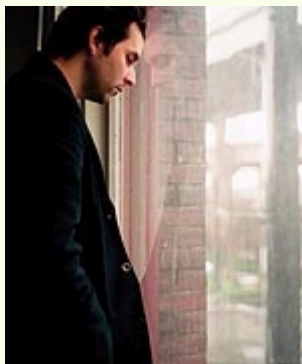
Exciting research also indicates a possible therapeutic role for vitamin D in preventing diabetes.

Vitamin D supplementation may reduce susceptibility to type II diabetes by slowing the loss of insulin sensitivity in people who show early signs of the disease. Researchers studied 314 adults without diabetes and gave them either 700 IU of vitamin D and 500 mg of calcium daily or a placebo for three years.⁷³ Among subjects who had impaired (slightly elevated) fasting glucose levels at the study's onset, those taking the active supplement had a smaller rise in glucose levels over three years than did the controls, as well as a smaller increase in insulin resistance. The researchers concluded that for older adults with impaired glucose levels, supplementing with vitamin D and calcium may help avert metabolic syndrome and type II diabetes.

Type I (insulin-dependent) diabetes is an autoimmune condition, in which the body's immune system attacks its own insulin-producing pancreatic beta cells. Low vitamin D levels are associated with the development of autoimmune conditions,^{40,74,75} including type I diabetes,³⁸ and scientists have proposed that vitamin D supplementation may help prevent the disease.⁷⁶

A very large population-based study in Europe demonstrated the powerful effect of vitamin D supplementation in protecting children against the development of type I diabetes.⁷⁷ Data from 820 diabetics and 2,335 non-diabetic controls showed that children who received vitamin D supplements in infancy reduced their risk of developing type I diabetes by approximately 33%. The researchers believe that activated vitamin D may protect growing children from autoimmune attack on insulin-producing cells of the pancreas.

VITAMIN D MAY HELP ALLEVIATE DEPRESSION



It is well established that for people with major depression, symptoms tend to worsen in winter, and also that some people without baseline depression develop depressive symptoms in winter (so-called seasonal affective disorder, or SAD).^{94,95} Light therapy has been found to be useful for treating wintertime depressive symptoms,⁹⁶ and it seems likely that at least some of the benefit of light therapy is related to increased activation of vitamin D.

To test this idea, researchers conducted a randomized trial in 15 people with SAD.⁹⁵ Eight received a single dose of 100,000 IU of vitamin D, and seven received one month of light therapy. All of the supplemented patients—and none of the light-treated patients—had major improvement in depression scores. Interestingly, similar studies using much lower doses of 400-800 IU per day did not yield improvements in SAD symptoms,^{94,97} again suggesting that we simply need more vitamin D than has been thought.

Vitamin D's benefits for mental health may not be limited to depression. A 2004 study from Finland⁹⁸ showed that the risk of developing schizophrenia in adult men was greatly increased in those who had never had vitamin D supplementation as infants, compared to those who had had at least some supplementation. Another recent paper proposes that prenatal vitamin D deficiency could be linked to adult schizophrenia.⁹⁹ Finally, a laboratory study showed that prenatal vitamin D deprivation was associated with certain behaviors in adult rats that are typical of schizophrenia in humans.¹⁰⁰

VITAMIN D PROVIDES ESSENTIAL IMMUNE SUPPORT

Vitamin D appears to be essential in maintaining healthy white blood cells and a robust immune system.⁷⁵

A recent paper presented persuasive evidence that seasonal infections such as influenza may actually be the result of decreased vitamin D levels,²⁶ not of increased wintertime viral activity, which has been the longstanding conventional wisdom.⁷⁸ This makes sense, because vitamin D receptors are present on many of the immune system cells responsible for killing viruses and deadly bacteria, and the vitamin—which is less environmentally available in the winter—appears to be a requirement for proper activation of these cells.^{79,80}

A randomized, double-blind study published in 2006 found that vitamin D may support recovery from tuberculosis, a common and deadly infection that most commonly affects the lungs. When patients with moderately advanced tuberculosis supplemented with 0.25 mg (10,000 IU) per day of vitamin D for one week, they had significantly higher rates of improvement than patients who received a placebo.⁸¹

Kidney dialysis patients often demonstrate decreased vitamin D levels as well as impaired cellular immune response. Dialysis patients with decreased vitamin D levels and impaired function of anti-viral and anti-cancer natural killer cells experienced substantial increases in natural-killer-cell activity after just one month of supplementation with prescription vitamin D (calcitriol) at 0.5 mcg (20 IU) per day.²⁷ In the laboratory, the same researchers demonstrated that vitamin D treatment of “generalized” white blood cells called monocytes caused them to mature into active natural killer cells within 24 hours.

Further evidence of vitamin D’s ability to bolster protective immune function comes from a laboratory study published earlier this year.⁸² Researchers discovered that skin cells responding to injury require vitamin D3 to “switch on” vital proteins involved in recognizing and responding to the microbes that cause wound infections. This finding has tremendous implications for preventing and treating wound infections.



CONCLUSION

Even in people who take vitamin D supplements, the percentage of those with sub-optimal levels remains surprisingly high. Humans cannot arbitrarily consume massive doses of vitamin D (unlike water-soluble nutrients such as vitamin C). For this nutrient, individualized dosing is of particular importance, and the only way to accomplish this is through vitamin D blood testing. With deficiencies likely to be most pronounced following the long winter months, spring is an excellent time to investigate your own vitamin D status.

Detecting deficient levels allows you and your physician to implement vitamin D supplementation to help avert illnesses associated with inadequate vitamin D levels. Optimizing your vitamin D intake may be a safe, low-cost way to protect against cancer, cardiovascular disease, diabetes, immune disorders, and depression, among other serious health conditions.

VITAMIN D BASICS

Vitamin D occurs in nature in two main forms: vitamin D2, or ergocalciferol, and vitamin D3, or cholecalciferol. While vitamin D2 is obtained from plant sources, vitamin D3 can be either obtained through animal sources, supplements, or synthesized in the skin when its precursor molecule absorbs light energy from ultraviolet B rays.⁸³

In the liver, both vitamin D2 and vitamin D3 are converted into 25-hydroxy-vitamin D, the primary circulating form of vitamin D. Conversion into its active form, 1,25-dihydroxyvitamin D, occurs in the kidney. Pharmaceutical drug forms of activated vitamin D include calcitriol, doxercalciferol, and calcipotriene.⁸³

Supplemental vitamin D is available as vitamin D2 (ergocalciferol) or vitamin D3 (cholecalciferol). Vitamin D2 is only about 20-40% as effective as D3 in maintaining serum concentrations of 25-hydroxyvitamin D, since it is more rapidly broken down in the body. For this reason, vitamin D3 (cholecalciferol) supplements are considered more beneficial than vitamin D2 (ergocalciferol) supplements.⁷

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