

**Medscape 12 Feb 2013**

### **Explosion of Research**

The number of research studies on vitamin D has soared in recent years. Citations of studies involving vitamin D increased from 1142 in the year 2000 to 3877 in 2012. In comparison, citations for research on vitamin A and vitamin C have remained more or less level. The sun may not be the best way to get vitamin D, but the evidence may yet show that vitamin D is the best thing under the sun.

### **The Vitamin That's Not a Vitamin**

The fourth vitamin to be discovered, vitamin D is a group of secosteroid compounds that include ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). The term "vitamin" is generally reserved for vital substances the body cannot synthesize on its own. Given cholesterol and sunshine, the body can synthesize its own vitamin D, so it's not technically an essential dietary vitamin. Serious deficiencies in vitamin D can lead to rickets, and it was research into this childhood disease, the pediatric form of osteomalacia, that led to the vitamin's 1922 discovery by Edward Mellanby.

### **Vitamin D and Bone**

Vitamin D has long been known to play an important role in bone health, and several recent studies provided additional confirmation. One study suggested that low levels of vitamin D increase the risk for forearm fracture in children, and another showed that girls who consumed the most vitamin D had the lowest risk for stress fractures. It's not just children who are at risk: 44% of postmenopausal women treated for distal radius fracture were vitamin D deficient or insufficient. And a meta-analysis showed that high doses of vitamin D lower the risk for fracture by 14% to 30% in people age 65 years or older.

### **Vitamin D and Respiratory Infections?**

If Linus Pauling were alive today, perhaps he would turn his attention away from vitamin C and write "Vitamin D and the Common Cold."

One randomized controlled trial suggested that vitamin D supplementation reduced acute respiratory tract infections in children during the long, cold, and dark Mongolian winter. Another randomized controlled trial showed that vitamin D reduced symptoms and antibiotic use in a group of patients with an increased frequency of respiratory infections. On the other hand, a third randomized controlled trial showed no effect of vitamin D on reducing the incidence or severity of respiratory infection in healthy adults.

### **Links to Diabetes**

Low levels of vitamin D have been linked to several types of diabetes. A study conducted in Australia found that children with type1 diabetes are more likely to have low levels of vitamin D. It's unclear, however, whether low levels of vitamin D caused the diabetes or vice versa. A larger study, in active-duty military personnel in the United States, found that those with low levels of vitamin D were more likely to develop insulin-requiring diabetes within 1 year. And women who have low vitamin D levels during their first trimester of pregnancy were more likely to develop gestational diabetes.

### **Vitamin D and Cardiovascular Disease**

Numerous epidemiologic studies, including the largest one to date, suggest that a low vitamin D level increases the risk for cardiovascular disease. But there may be a threshold effect, with heart health improving as circulating vitamin D levels increase from 20 to 60 nmol/L, followed by a plateau or perhaps even an increase in risk at higher levels. Unfortunately, a randomized controlled trial among older women failed to find evidence that vitamin D supplementation improved markers of heart health.

## **Obesity**

Women with low levels of vitamin D during pregnancy may have children that are more prone to excess body fat at age 6 years. Furthermore, children ages 6 to 18 years who are overweight are more likely to have low vitamin D levels. Adequate levels of vitamin D are associated with less weight gain among women age 65 and older.

## **Vitamin D and Cancer**

Less information has been published about connections between vitamin D and cancer, but some developments have occurred in the past year. In a result the researchers termed "unexpected," women with breast cancer who were being treated with zoledronic acid for bone complications had a lower risk for bone recurrence if they had sufficient vitamin D levels. Vitamin D supplementation may help breast cancer survivors adhere to adjuvant treatment with aromatase inhibitors. And differences in vitamin D-related genes may contribute to increased susceptibility to colon cancer among black Americans.

## **Neurologic Function**

Vitamin D has been tied to several higher neurologic functions. Studies have linked autism to low vitamin D during pregnancy, a connection that was strengthened by a map showing that autism rates were highest among children living in states with the lowest levels of ultraviolet B radiation. People with Alzheimer's disease tend to have low levels of vitamin D, and better cognitive test results are linked to higher vitamin D levels. Vitamin D<sub>3</sub> may help clear the brain of amyloid- $\beta$ . And low vitamin D levels in pregnant women have been associated with poor language development in their offspring.

## **Stroke and Multiple Sclerosis**

Data from the Honolulu Heart Program show that people with low dietary vitamin D at baseline were about 25% more likely to sustain thromboembolic stroke, but not hemorrhagic stroke, during the ensuing 34 years.

The last year has seen a flurry of studies linking vitamin D to multiple sclerosis (MS), and all of them tie low levels of vitamin D to the disease. Three of these studies were published in a single issue of the journal *Neurology*. Another study linked low levels of vitamin D plus exposure to the Epstein-Barr virus to the development of MS. Low vitamin D levels predict a near-term conversion of clinically isolated syndromes to definite MS. And the risk of developing MS has been linked to lower sun exposure in early life.

## **Pain**

About half of women prescribed aromatase inhibitors for metastatic breast cancer suffer intense musculoskeletal pain, but high-dose vitamin D<sub>2</sub> supplements appear to help. A single oral dose of 300,000 IU of vitamin D appears to help with dysmenorrhea. And a low level of vitamin D in black Americans increases the risk for knee osteoarthritis pain.

## **Lung Disorders**

High-dose vitamin D may speed tuberculosis recovery. And low vitamin D levels appear to be linked to the need for steroids in asthma and may also blunt the effectiveness of asthma treatment.

For chronic obstructive pulmonary disease, however, the story isn't as clear cut. According to one study, high-dose vitamin D supplementation improves exercise capacity and respiratory muscle strength during rehabilitation. But according to another, high-dose supplements failed to prevent exacerbations or secondary outcomes.

## **Gastrointestinal Disorders**

Women with sufficient vitamin D levels at baseline are 62% less likely to develop Crohn's disease over 22 years than those with vitamin D insufficiency.

Women living at southern latitudes in the United States are 52% less likely to have inflammatory bowel disease than those living in the north.

### **Kidney Disease**

Vitamin D deficiency is almost universal among patients with chronic kidney disease (CKD). Two recent studies independently concluded that high-dose cholecalciferol (vitamin D3) supplementation safely prevents and corrects this in patients undergoing dialysis. Vitamin D supplementation also lowers hepcidin levels in patients with CKD.

### **But Wait, There's More**

Within the past year, studies have shown that vitamin D may reduce risk for dental caries, low vitamin D may be a result of depression, vitamin D deficiency increases risk for perforated eardrums, and low vitamin D is linked to food allergy. And the list goes on.

### **How Much Is Enough?**

There's little consensus about what blood levels of vitamin D are adequate, and even less on how much supplementation is enough. The Institute of Medicine says blood levels should be 20 ng/mL, but the Endocrine Society sets the level at 30 ng/mL. The US Recommended Dietary Allowance is 600 IU for people ages 1 to 70 years and 800 IU for those who are older. Some authorities recommend that people who are deficient should receive supplements of 1000 to 2000 IU daily, but others have recommended single-bolus doses of up to 500,000 IU.

### **How to Measure?**

If there's little agreement on how much vitamin D we need, there's even less on how to measure blood levels. You can choose an old, slow, but accurate method, or you can choose one of several new and fast but wildly inaccurate methods. According to one study, these rapid tests may be inaccurate as much as 40% of the time, most often characterizing patients as vitamin D deficient when they're not.

### **Elixir of Life?**

While vitamin D appears to be involved in almost every body system, some researchers are looking at the big picture — overall mortality. Oral active vitamin D is associated with reduced all-cause mortality in patients undergoing peritoneal dialysis. Vitamin D has also been linked to lower mortality in patients with pneumonia. And a large meta-analysis found that increased intake of vitamin D plus calcium, but not vitamin D alone, is linked to a decrease in all-cause mortality among elderly patients.

### **And Now for Something Completely Different**

So if you've been paying attention to the previous slides, they nearly all seem to point in one direction: Lower levels of vitamin D bad, higher levels good or neutral. Case closed? Maybe not. A recent study suggests that some people with a genetic predisposition to longevity have a reduced frequency of a gene variant that predisposes people to high vitamin D levels. They also have lower levels of vitamin D. If only science gave us simple, unambiguous answers!

### **For more information:**

#### **Vitamin D and Bone**

[Low Vitamin D Linked to Forearm Fracture Risk in Children](#)

[Lower Stress Fracture Risk in Girls Linked to Vitamin D Intake](#)

[Nearly Half of Older Women With Arm Fractures Have Low Vitamin D](#)

[High Vitamin D Doses Lower Fracture Risk for Most Vulnerable](#)

#### **Vitamin D and Respiratory Infections**

[Vitamin D Supplementation Cuts Respiratory Infections](#)

[Vitamin D May Reduce Respiratory Infection Symptoms](#)

[Vitamin D Ineffective for Respiratory Tract Infections](#)

### **Vitamin D and Diabetes**

[Lower Vitamin D Levels Linked to Type 1 Diabetes](#)

[Diabetes Risk Linked to Low Vitamin D Levels](#)

[Low First-Trimester Vitamin D Predicts Gestational Diabetes](#)

### **Vitamin D and Cardiovascular Disease**

[Largest Epidemiologic Study to Date Links Low Vitamin D to CVD Risk](#)

[New Meta-Analysis Suggests 'Threshold' Effect for Vitamin D and CVD](#)

[Vitamin D Supplements May Not Improve Heart Health](#)

### **Vitamin D and Obesity**

[Low Maternal Vitamin D May Lead to Higher Body Fat in Kids](#)

[Overweight Kids More Likely to Be Deficient in Vitamin D](#)

[Vitamin D Linked to Modest Decrease in Weight Gain](#)

### **Vitamin D and Cancer**

[Vitamin D: 'Surprise' Prognostic Marker in Breast Cancer](#)

[Vitamin D May Help Breast Cancer Survivors Stay on Track](#)

### **Vitamin D and Neurologic Function**

[More Evidence Vitamin D May Reduce Autism Risk](#)

[Low Vitamin D Linked to Alzheimer's Disease](#)

[Studies Show How Vitamin D3 Helps Clear Amyloid in AD](#)

[Prenatal Vitamin D May Influence Kids' Language Skills](#)

### **Vitamin D and Stroke/Multiple Sclerosis**

[Low Vitamin D in Diet Linked to Increased Stroke](#)

[Vitamin D Linked to Disease Activity in MS](#)

[Low Vitamin D, Epstein-Barr, Linked to Later MS](#)

[MS Risk Linked to Low Sun Exposure Early in Life](#)

### **Vitamin D and Pain**

[Vitamin D Improves Pain From Aromatase Inhibitors](#)

[Can Vitamin D Treat Pain?](#)

[Osteoarthritis Knee Pain Linked to Vitamin D, Race](#)

### **Vitamin D and Lung Disorders**

[High-Dose Vitamin D May Speed Recovery From Tuberculosis](#)

[Low Vitamin D Linked to High IgE, Need for Steroids in Asthma](#)

[Low Vitamin D May Blunt Effectiveness of Asthma Treatment](#)

[Vitamin D Supplementation Boosts COPD Rehabilitation](#)

[High-Dose Vitamin D Fails to Mitigate COPD Exacerbations](#)

### **Vitamin D and Gastrointestinal Disorders**

[Vitamin D May Decrease Risk for Crohn's Disease](#)

[Less Inflammatory Bowel Disease Seen in Southern Latitudes](#)

### **Vitamin D and Kidney Disease**

[Vitamin D Deficiency Likely Among Many Patients Starting Dialysis](#)

[High-Dose Cholecalciferol Prevents Vitamin D Insufficiency in Kidney Disease](#)

[Vitamin D Deficiency Safely Corrected in Dialysis Patients](#)

[Vitamin D Lowers Heparin Levels in CKD Patients](#)

### **Vitamin D and Other Disorders**

[Vitamin D Supplements May Reduce Risk for Dental Caries](#)

[Low Vitamin D a Result, Not a Cause, of Depression](#)

[Vitamin D Deficiency Linked With Eardrum Perforation Risk](#)

[Infant Food Allergy Linked to Low Vitamin D](#)

### **How Much Is Enough, and How Best to Measure Blood Levels?**

[Vitamin D Consensus Remains Elusive Despite Recommendations](#)

[Sun Exposure Not Enough to Correct Vitamin D Deficiency](#)

[Newer Vitamin D Tests Often Inaccurate: Study](#)

**Vitamin D and Overall Mortality**

[Patients on Peritoneal Dialysis May Benefit From Vitamin D](#)

[Vitamin D Levels Linked to Mortality in Patients With Pneumonia](#)

[Vitamin D With Calcium May Reduce Mortality in Elderly](#)

[Low Vitamin D Levels Linked to Longer Life](#)