

# NUTRITION ACTION

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HEALTH LETTER



## ARE YOU **D**EFICIENT?



### Too little vitamin D puts more than bones at risk

BY BONNIE LIEBMAN

**O**steoporosis, muscle weakness, gum disease, diabetes, insulin resistance, arthritis, multiple sclerosis, and cancers of the breast, colon, pancreas, and prostate.

That's a partial—and still growing—list of the illnesses that vitamin D may help prevent. How might one vitamin do so much?

Vitamin D isn't like any other vitamin. It's a hormone that has receptors in most—if not all—cells in the body. It affects how cells grow, proliferate, and "specialize," how the body makes bone, muscle, and insulin, and how the immune system fights disease...or itself.

And many experts are now convinced that we get far too little.

*Continued on page 3.*

# ARE YOU **D**EFICIENT?

**H**ow much vitamin D do we need?

It's been nearly 10 years since the Institute of Medicine issued the latest recommendations—200 to 600 International Units (IU) a day, depending on age. And those levels were based on how much it would take to prevent rickets, the disease characterized by bowed or deformed bones.

"There's been a huge amount of data since 1997," says researcher Bess Dawson-Hughes of the Jean Mayer U.S. Department of Agriculture Human Nutrition Research Center on Aging at Tufts University in Boston.

"The evidence has just exploded—not just on bones, but diabetes, infection, insulin resistance, various cancers," she adds. And it looks like we're getting too little vitamin D for all of them.

Most vitamins occur naturally in a variety of foods. Not vitamin D.

"Initially, humans didn't require vitamin D in their food supply," says researcher Bruce Hollis of the Medical University of South Carolina in Charleston, "because over millions of years we evolved a mechanism to produce it in our skin."

Relying on the sun's ultraviolet rays to make vitamin D worked fine when all humans lived near the equator. But "approximately 50,000 years ago, small bands of people, almost certainly darkly pigmented, migrated gradually from sub-Saharan Africa to more northern latitudes," Hollis explains.

Further from the equator, UV rays were scarce, leading to rickets, the vitamin D deficiency disease that deforms bone, including the pelvis. "Populations couldn't survive if they became ricketic because women couldn't deliver a child," says Hollis. "Both would die at birth."

Scientists suspect that the light-skinned races lost their skin pigment so they

could absorb more of the sun's UV rays.

"Northern populations became depigmented fast," explains Hollis, because the mutation that led to lighter skin had a huge survival advantage.

"People of color couldn't survive in

limited sun," he adds. The exception: Eskimos have endured, because they live on fatty fish, the only food that is rich in vitamin D.

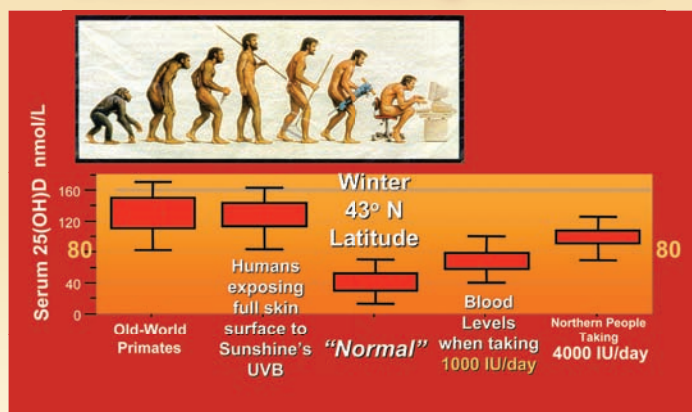
## BONES

Vitamin D helps the body absorb calcium, so it's no surprise that giving people vitamin D—with or without calcium—can boost the density of hip and some other bones (though it appears to have little impact on the spine).<sup>1</sup>

Does vitamin D actually keep bones from breaking? Yes, says Dawson-Hughes, "but only if you look at studies in which people took enough to get their blood levels high enough."

In a meta-analysis that pooled the results of those studies, people who took 700 to 800 IU a day had a 26 percent lower risk of hip fractures than similar people who took a placebo.<sup>2</sup>

## Vitamin D Status in Primates and Early Humans

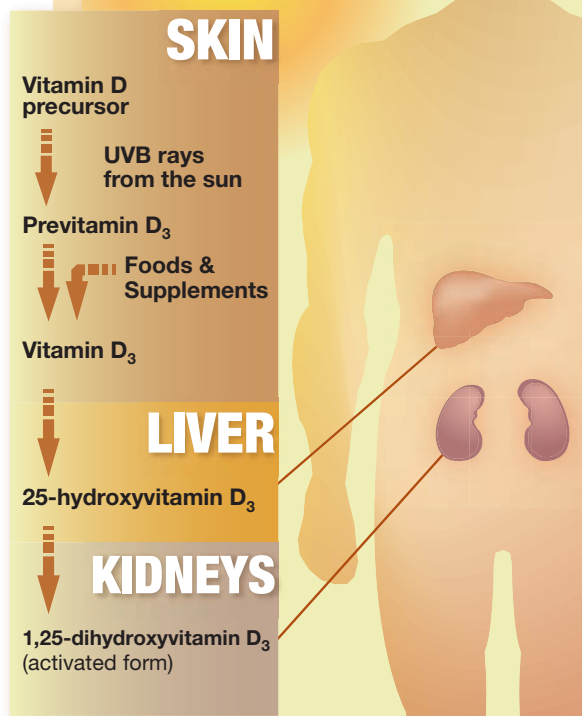


**Why take vitamin D?** Until recently, blood levels of vitamin D that are typical in a Boston winter (about 40 nanomoles per liter) were considered "normal." However, early humans had vitamin D levels closer to 130 nanomoles per liter because they were exposed to the sun's ultraviolet rays all day. Taking 1,000 IU of vitamin D a day (with no sun exposure) would bring those Boston blood levels up to about 80 nanomoles per liter. Taking 4,000 IU would bring them to 100 nanomoles per liter.

Courtesy Bruce Hollis. Sources include *Osteoporos. Int.* 11: 271, 2000; *N. Engl. J. Med.* 340: 1840, 1999; *Osteoporos. Int.* 8: S7, 1998; *Am. J. Clin. Nutr.* 69: 842, 1999.



## How the Body Makes Vitamin D



In the skin, sunlight converts a precursor of vitamin D to previtamin D<sub>3</sub>, which then turns into vitamin D<sub>3</sub> (also found in some foods and supplements). In the liver, vitamin D<sub>3</sub> is converted to 25-hydroxyvitamin D<sub>3</sub>, which is then converted to active vitamin D<sub>3</sub> in the kidneys and in some cells of the body.

In other studies, “the doses of vitamin D were similar, but there wasn’t a step up in blood levels of D,” notes Dawson-Hughes, probably because participants stopped taking the supplements.<sup>3</sup>

For example, in a British study of more than 5,000 older people who had already broken a bone, “the researchers gave 800 IU a day, but only half of the participants were taking any pills after two years of the five-year study,” she explains. “Compliance probably trailed off further after that.”

The bottom line: 1,000 IU of vitamin D a day could substantially lower the risk of broken bones in older people, says Dawson-Hughes. But, she adds, it’s not just vitamin D’s impact on bone that would ward off those fractures.

### MUSCLE

“Vitamin D affects bone mass and strength, but it also lowers the risk of falling by improving balance and muscle performance,” says Dawson-Hughes. “It’s a two-pronged benefit.”

Muscle tissue has receptors that are specifically designed to accept vitamin D, which suggests that the vitamin must have a key role in muscle function.

“When researchers gave vitamin D to older women, they saw an increase in protein synthesis, which means an increase in muscle growth and size,” Dawson-Hughes explains.

Older people with higher blood levels of vitamin D also do better on tests that require muscle strength and balance.<sup>4</sup> “The higher their vitamin D, the faster they can walk eight steps and get out of a chair,” she says. “It’s a very striking association.”

### GUMS

Periodontal disease is the leading cause of tooth loss, especially in older people. It’s caused by chronic inflammation, which leads to receding gums. Eventually, the tooth starts to wear away.

“Several studies have seen an association between low vitamin D levels and periodontal disease,” says Dawson-Hughes. “A link is also turning up with gingivitis, which is the precursor to periodontal disease.”<sup>5</sup>

In one trial, older people who were given vitamin D (700 IU a day) and calcium (500 mg a day) for three years had 60 percent less tooth loss than similar people who got a placebo.<sup>6</sup>

“Vitamin D may influence gum disease because it suppresses inflammation,” says Dawson-Hughes. “It warrants more work.”

### CANCER

“The animal studies are pretty remarkable,” says cancer expert Edward Giovannucci of the Harvard School of Public Health in Boston. When animals are given vitamin D, “researchers see a dramatic reduction in tumor growth.”

Vitamin D appears to make cancer cells less abnormal, less likely to multiply, and more likely to die. It also tunes up the immune system.

What’s more, vitamin D may hinder angiogenesis, the growth of new blood vessels

that feed a tumor. “And there’s evidence that vitamin D may make cancer cells adhere to the tumor, which could keep them from branching out and becoming metastatic,” he adds.

“Hundreds of studies in test tubes and animals show strong effects on many kinds of tumors,” says Giovannucci. “They’re very impressive, but we’re not sure if they’ll transfer to humans.”

In people, the evidence is more complex. For example, researchers at Harvard reported a lower risk of colorectal cancer in women with higher vitamin D levels in their blood, but only in those over 60.<sup>7</sup> Another study, testing blood samples from 800 people, found a lower risk of precancerous colon polyps in women—but not men—with higher vitamin D levels.<sup>8</sup>

“The evidence is most consistent for colon cancer,” explains Giovannucci. “Prostate cancer is puzzling because the results are not consistent. And there just aren’t many studies for breast cancer.”

A study that analyzed blood samples from roughly 1,400 women found a lower risk of breast cancer in those with the highest vitamin D levels, but only if the women were over 60.<sup>9</sup> And in a British study, low vitamin D levels were linked to a higher risk of breast cancer only in women with one variation of a gene that affects vitamin D receptors.<sup>10</sup>

Giovannucci and others aren’t discouraged by recent results from the Women’s Health Initiative, a massive trial that found no difference in colon or breast cancer rates between women who took a placebo and women who took vitamin D (400 IU a day) and calcium (1,000 mg a day).

“The vitamin D dose was way too low,” he explains. “And many of the women who got a placebo were taking their own vitamin D and calcium supplements, so there wasn’t much difference between the two groups.”

Supplements aside, women who entered the trial with higher vitamin D levels in their blood had a lower risk of colon cancer during the seven-year study.<sup>11</sup> (The researchers haven’t looked at breast cancer rates in those women.)

The latest finding: When scientists analyzed the foods and supplements consumed by



roughly 46,000 men and 75,000 women, those who got at least 600 IU a day of vitamin D had a 40 percent lower risk of pancreatic cancer than those who got less than 150 IU a day.<sup>12</sup> This time, the link between vitamin D and cancer was stronger in men than in women.

"I don't want to go overboard, but vitamin D is the most promising of anything I've seen in nutrition that can potentially have a strong effect on cancers," says Giovannucci.

"But whether the results from animal studies will transfer to humans, we don't know. It's not a cure-all, and we still have a lot of work to do."

### INSULIN & DIABETES

"Promising but not definitive."

That's how Anastassios Pittas of the Tufts-New England Medical Center in Boston describes the evidence that vitamin D can lower the risk of diabetes.

A study that looked at a nationally representative sample of the U.S. population found a 75 percent lower risk of diabetes in non-Hispanic whites with the highest blood levels of vitamin D than in those with the lowest levels.<sup>13</sup>

"But we can't be sure if diabetes was causing low vitamin D levels or the other way around," explains Pittas.

Perhaps more compelling are the results of his recent study on roughly 300 people aged 65 or older, a third of whom had pre-diabetes—that is, their blood sugar levels were higher than normal but not high enough to warrant a diagnosis of diabetes.

Among those with pre-diabetes, fasting blood sugar levels went up significantly less over three years if the people were given vitamin D (700 IU a day) and calcium (500 mg a day) than if they got a placebo.<sup>14</sup>

But the calcium and vitamin D had no effect on people who started the study with normal blood sugar levels.

"It's nearly impossible to separate the individual effects of each nutrient, partly because one function of vitamin D is to help the body absorb calcium," says Pittas.

Other lines of evidence are tantalizing.

"Research suggests that vitamin D promotes insulin secretion from the beta islet cells in the pancreas," says Pittas. "And it might influence insulin resistance."

All things considered, he concludes,



## Where's the D?

Your skin makes vitamin D when it's exposed to the sun's ultraviolet rays (unless you're wearing sunscreen). But north of the line running roughly between Los Angeles and Atlanta, the UV light is too weak to make vitamin D from late fall through early spring (see "The Winter Sun," p. 6).

Solution: ignore the sun (and sunscreen, latitude, and season) and simply take 1,000 IU a day of vitamin D<sub>3</sub> (which is more potent than vitamin D<sub>2</sub>). You can use this chart to figure out how much vitamin D you're already getting from your multivitamin (probably 400 IU), calcium supplement (perhaps 100 IU), milk (100 IU per cup), or yogurt (a few brands have 80 IU per 6 oz. tub). You'll probably need to take the remainder as a separate vitamin D supplement.

Labels on supplements and fortified foods list vitamin D as a percentage of the Daily Value, or DV, which is 400 IU. So a food with 40% of the DV has 160 IU.

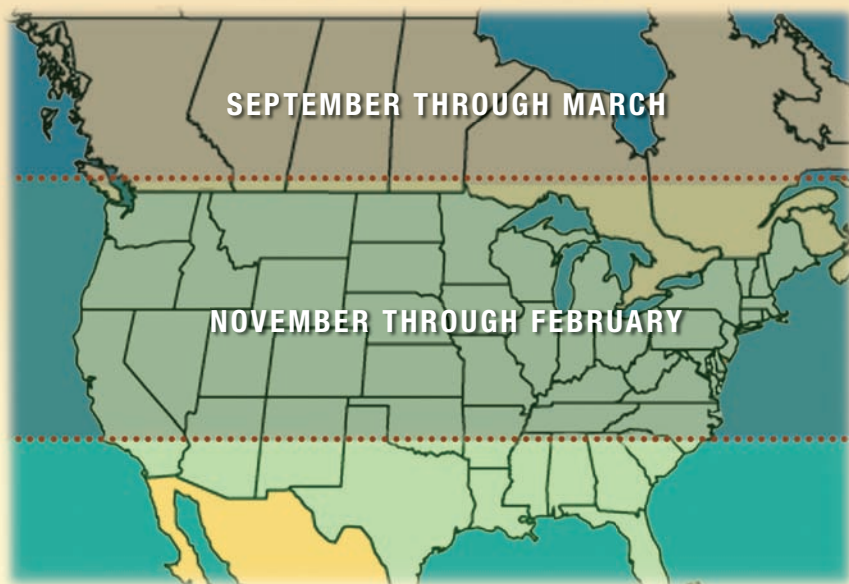
Food or Supplement	Vitamin D (IU)*
Catfish (3 oz. cooked)	570 <sup>1</sup>
Red (sockeye) salmon, canned (1/4 cup)	480 <sup>1</sup>
Multivitamins, most brands	400
Pink salmon, canned (1/4 cup)	290 <sup>1</sup>
Shrimp (3 oz. cooked)	170 <sup>1</sup>
Dannon Frusion Smoothie (10 oz.)	140
Quaker Oatmeal Nutrition for Women (1 packet)	140
Slim-Fast shake (1 can—11 oz.)	140
Tuna, light, canned in water or oil (1/4 cup) <sup>#</sup>	130 <sup>1</sup>
Silk Soymilk (1 cup)	120 <sup>2</sup>
Ensure (1 can or bottle—8 oz.)	100-140
8th Continent Soymilk (1 cup)	100 <sup>2</sup>
Milk (1 cup)	100
Minute Maid Calcium + D Orange Juice (1 cup)	100
Tropicana Calcium + Vitamin D Orange Juice (1 cup)	100
Viactiv Calcium Soft Chews (1 chew)	100
Yoplait Nouriche SuperSmoothie (11 oz.)	100
Dannon Light 'n Fit Nonfat Yogurt (6 oz.)	80
Yoplait Yogurt (6 oz.)	80
Country Crock Plus Calcium & Vitamins spread (1 Tbs.)	60
I Can't Believe It's Not Butter! Sweet Cream & Calcium spread (1 Tbs.)	60
Breakfast cereal, most brands (3/4-1 cup)	40
Edensoy Extra or Light Soymilk, Original or Vanilla (1 cup)	40 <sup>2</sup>
Parkay Calcium spread (1 Tbs.)	40
Sara Lee Heart Healthy Plus bread (1 slice)	40
Egg Beaters (1/4 cup)	20-40
Egg (1)	20 <sup>1</sup>
Edensoy Soymilk, Original, Vanilla, Chocolate, or Carob (1 cup)	0

\*The vitamin D in most foods and many supplements is the D<sub>3</sub> form (cholecalciferol), which is usually derived from animal sources. Fortified soy milks and some supplements contain less-potent vitamin D<sub>2</sub> (ergocalciferol), which is usually derived from yeast.

<sup>1</sup>Naturally occurring. <sup>2</sup>Vitamin D<sub>2</sub>. <sup>#</sup>There are no reliable numbers for white (albacore) tuna.

Sources: U.S. Department of Agriculture, company information.

## The Winter Sun



**There goes the sun.** In most of the United States, people can't make vitamin D from the sun from November through February.

"the evidence is preliminary but intriguing enough to study further."

Another interesting link: many diabetics are overweight, which increases the body's need for vitamin D.

"It's well established that the higher the body mass index, the lower the levels of vitamin D," explains Pittas. "The thought is that vitamin D is fat-soluble so it's sequestered in fat, leaving less in blood in people who are overweight."

That makes it even more critical for the overweight to get enough vitamin D.

### IMMUNE SYSTEM

"A vitamin D deficiency hampers the immune system," says researcher Bruce Hollis of the Medical University of South Carolina.

That may explain why "sun exposure in sanitariums cured tuberculosis 100 years ago," he adds. Immune system cells called macrophages have the machinery to make the active form of vitamin D, which gets the macrophages busy making peptides that fight bacteria.

"If you're deficient in vitamin D, that can't happen," says Hollis. "People's bodies couldn't destroy the TB bacteria." That might also explain why African Americans are more susceptible to TB, he adds. The pigment in their skin leads to lower vitamin D levels in their blood.<sup>15</sup>

Scientists are also investigating vita-

min D's impact on autoimmune diseases.

"Vitamin D decreases the production of T-1 helper cells and enhances the formation of T-2 helper cells," says Hollis. That's good because T-1 cells are involved in autoimmune attacks on the body.

Among the autoimmune disorders under study:

■ **Type 1 diabetes.** The common Type 2 diabetes is linked to obesity. Type 1 diabetes, which usually strikes in childhood, is an autoimmune disease that's triggered when the immune system attacks cells in the pancreas that make insulin.

Vitamin D slashed the incidence of Type 1 diabetes in mice that are predisposed to get the disease.<sup>16</sup> And children who were recently diagnosed had lower blood levels of vitamin D than others.<sup>17</sup> Researchers in Finland are giving infants at high risk of Type 1 diabetes daily doses of 2,000 IU of vitamin D to see if it can ward off the disease.<sup>18</sup>

"I think the evidence on Type 1 diabetes is so strong that I give vitamin D to my kids," says Tufts' Anastassios Pittas.

■ **Multiple sclerosis.** Researchers found a 40 percent lower risk of MS in women who took at least 400 IU of vitamin D a day.<sup>19</sup> "A new study had similar, and stronger, findings in military personnel," says Hollis.

■ **Rheumatoid arthritis.** Vitamin D levels are often low in patients with rheuma-

toid arthritis, and that may hinder macrophages from churning out the active form of vitamin D, which seems to temper an overactive immune system. Researchers at Penn State University are giving patients 1,000 IU of vitamin D a day to see if it curbs their inflammation.<sup>20</sup>

### OSTEOARTHRITIS

An estimated 43 million Americans—one out of five adults—have been diagnosed with arthritis. The disease is responsible for 750,000 hospitalizations, 36 million doctor visits, \$51 billion in medical costs, and 9,500 deaths each year. By far, the most common type of arthritis is osteoarthritis.

And so far, no one knows how to stop cartilage—which is supposed to protect bones—from wearing away, leaving hips, knees, and other joints feeling stiff and sore.

Researchers got one of the first hints that vitamin D might help from a 1996 study that tracked more than 500 residents of Framingham, Massachusetts, for eight years.<sup>21</sup>

"Arthritis of the knees was about three times more likely to progress in people with the lowest blood levels of vitamin D," says arthritis expert Timothy McAlindon of the Tufts-New England Medical Center.

"And a study in San Francisco found that people with low levels of vitamin D were more likely to develop osteoarthritis of the hip," he adds. So, even though some studies have found no link with vitamin D, he says, "it seems like there's some smoke there."

Why? It's possible that people with low levels of vitamin D have lower quality bone, says McAlindon. And that leads to the bone spurs that can cause arthritis pain.

There's also a link with cartilage. "When bones stop growing, cartilage cells lose the vitamin D receptors they had during childhood," he explains. "But when a person has arthritis, the cartilage cells are stressed and vitamin D receptors reappear. That tells us that vitamin D might be doing something with cartilage as well as with bone."

McAlindon and his colleagues are now giving roughly 140 patients with arthritis of the knees a daily dose of 2,000 IU of vitamin D. After two years, they'll see if the vitamin has slowed the disease.

"Even if it's only modestly effective,

vitamin D could have considerable impact on the societal burden of osteoarthritis," notes McAlindon.

### HOW MUCH IS ENOUGH?

Most experts agree that it's time to raise the vitamin D intakes that are now recommended: 200 IU a day if you're 50 or under, 400 IU if you're 51 to 70, and 600 IU if you're over 70.

"There was no evidence at all for the current recommendations," says researcher Bruce Hollis. "They knew that 400 IU—the amount in a teaspoon of cod liver oil—would cure rickets in a child. Then they made the mistake of applying the same amount to adults."

Also shaky is the highest level of vitamin D that's safe to take on a daily basis (the Tolerable Upper Intake Level), which is 2,000 IU.

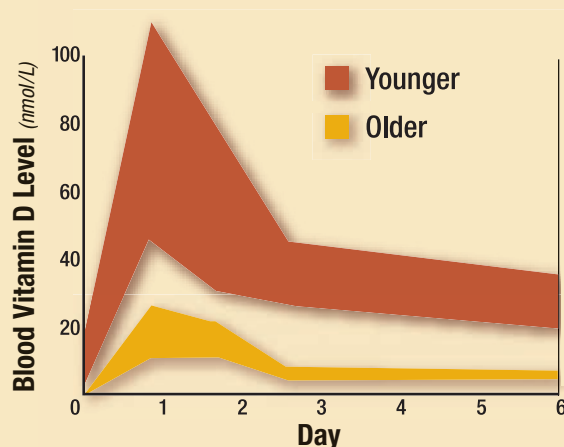
"That level was based on a 1984 study of six patients in India, and the researchers never measured the patients' blood levels," says Hollis. "It's horrific data that shouldn't be used."

He's now giving 4,000 IU a day to pregnant women and 6,000 IU a day to breastfeeding women in studies that are sponsored by the National Institutes of Health and sanctioned by the Food and Drug Administration.

"We haven't had one adverse event in 2½ years," he points out. "You need tens of thousands of units to get toxicity."

The key risk is that too much vitamin D will cause the body to absorb too much calcium, which can cause kidney damage. "But we see no perturbations in urinary

## More Years, Less D



**Young and full of D.** People aged 22 to 30 make more vitamin D than people aged 62 to 80 after being exposed to the same amount of sunlight.

Source: *Am. J. Clin. Nutr.* 60: 619, 1994.

calcium levels with doses up to 10,000 IU a day of vitamin D," says Hollis.

Another potential risk: in the Women's Health Initiative, researchers found a slightly increased risk of kidney stones in those who were given 400 IU of vitamin D and 1,000 mg of calcium a day.

But many of those women were really getting roughly 800 IU of vitamin D and 2,200 mg of calcium a day, because they were allowed to take their usual supplements along with the (unlabeled) pills that the researchers gave them.

That hasn't stopped some experts from recommending higher intakes.

"We could easily recommend 1,000 IU a day," says Tufts' Bess Dawson-Hughes.

"That would bring the average older person to an adequate level of 75 nanomoles per liter of blood."


But because some people need more than others, she adds, "we'd have to recommend 3,000 to 4,000 IU a day to get those blood levels in 98 percent of the population." And, she adds, higher blood levels—closer to 90 nanomoles per liter—may be even better.<sup>22</sup>

Those intakes appear to be safe. "It looks like if you give people more than 4,000 to 10,000 IU, the body stops converting vitamin D to its active form," says Pittas.

The bottom line: researchers are convinced that we should be getting as much vitamin D as lifeguards, not office workers.

"A light-skinned person out in the sun in a bathing suit, with no sunscreen, can make 20,000 to 30,000 IU in 30 minutes,"

explains Harvard's Edward Giovannucci, though a person with darker skin or less skin exposed would make much less.

"Perhaps unknowingly, most of us have been deficient compared to conditions under which people evolved," he adds. "Estimates are that most humans evolved with vitamin D levels of 125 to 175 nanomoles per liter of blood. A lot of people today are at 12 to 25 nanomoles." 

## D Bottom Line

- It's easier to get vitamin D from a supplement or fortified food than to worry about whether you're getting enough (or too much) sun.
- Shoot for about 1,000 IU of vitamin D a day. Check "Where's the D?" (p. 5) to see how much you get from a multivitamin, calcium supplement, milk, or other foods. Then look for a separate supplement to get the rest.
- If you take a vitamin D supplement, look for vitamin D<sub>3</sub> (also called cholecalciferol), not vitamin D<sub>2</sub> (also called ergocalciferol), which is about 25% less potent.
- It's safe to take up to 2,000 IU—some researchers would say 4,000 IU—a day. But if you're prone to kidney stones, check with your doctor before taking more than 1,000 IU a day.

<sup>1</sup> *J. Clin. Endocrinol. Metab.* 80: 1052, 1995.

<sup>2</sup> *JAMA* 293: 2257, 2005.

<sup>3</sup> *Lancet* 365: 1621, 2005.

<sup>4</sup> *Am. J. Clin. Nutr.* 80: 752, 2004.

<sup>5</sup> *Am. J. Clin. Nutr.* 82: 575, 2005.

<sup>6</sup> *Am. J. Med.* 111: 452, 2001.

<sup>7</sup> *Cancer Epidemiol. Biomarkers Prev.* 13: 1502, 2004.

<sup>8</sup> *Cancer Epidemiol. Biomarkers Prev.* 13: 546, 2004.

<sup>9</sup> *Cancer Epidemiol. Biomarkers Prev.* 14: 1991, 2005.

<sup>10</sup> *Eur. J. Cancer* 41: 1164, 2005.

<sup>11</sup> *N. Eng. J. Med.* 354: 684, 2006.

<sup>12</sup> *Cancer Epidemiol. Biomarkers Prev.* 15: 1688, 2006.

<sup>13</sup> *Diabetes Care* 27: 2813, 2004.

<sup>14</sup> 66th Scientific Sessions of the American Diabetes Association 2006, Abstract 327-OR.

<sup>15</sup> *Science* 311: 1770, 2006.

<sup>16</sup> *Diabetologia* 37: 552, 1994.

<sup>17</sup> *Horm. Metab. Res.* 37: 680, 2005.

<sup>18</sup> 66th Scientific Sessions of the American Diabetes Association 2006, Abstract 1790-P.

<sup>19</sup> *Neurology* 62: 60, 2004.

<sup>20</sup> [clinicaltrials.gov/ct/show/NCT00279461](http://clinicaltrials.gov/ct/show/NCT00279461).

<sup>21</sup> *Ann. Intern. Med.* 125: 353, 1996.

<sup>22</sup> *Am. J. Clin. Nutr.* 84: 18, 2006.