

The vitamin D miracle: Is it for real?

The claims have been sensational. Martin Mittelstaedt checks up on the research behind the hype

MARTIN MITTELSTAEDT
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In the summer of 1974, brothers Frank and Cedric Garland had a heretical brainwave.

The young epidemiologists were watching a presentation on death rates from cancer county by county across the United States. As they sat in a lecture hall at Johns Hopkins University in Baltimore looking at the colour-coded cancer maps, they noticed a striking pattern, with the map for colon cancer the most pronounced.

Counties with high death rates were red; those with low rates were blue. Oddly, the nation was almost neatly divided in half, red in the north and blue in the south. Why, they wondered, was the risk of dying from cancer greater in bucolic Maine than in highly polluted Southern California?

The two had arrived at Johns Hopkins a few days earlier, having driven their Mustang from their hometown of San Diego. Frank was about to begin graduate studies and Cedric his first job as a professor. It was July, and the trip through the sunny South gave them an idea as they studied the cancer maps: Exposure to sunshine varies dramatically depending on the latitude. What if that's what was behind the varying cancer rates?

Their hypothesis, painstakingly developed and published six years later in the *International Journal of Epidemiology*, was that sunlight has a powerful anti-cancer effect through its role in producing vitamin D in bare skin. Those living at northern latitudes, they theorized, receive less sunlight and make less of the vitamin, which in turn increases their risk of dying from cancer.

Today, with vitamin D so much in the news, it's hard to believe that it took decades for the Garlands' hypothesis to gain traction in the mainstream medical community.

But the benefits of vitamin D are no longer restricted to cancer prevention: Studies have linked a shortage of the compound to such serious, chronic ailments as multiple sclerosis, diabetes, heart disease, influenza and schizophrenia.

Cedric Garland, now a professor of preventive medicine at the University of California, San Diego, is so convinced of this broad link that he says, "I think vitamin D is introducing a golden age in medicine."

And he's not alone. So compelling is the latest research that a number of credible medical researchers and public-health advocates, many of them in Canada, have started taking doses far above 200 to 600 international units - the daily intake recommended by Health Canada, depending on age with an upper limit of 2,000 IU.

Canada's leading vitamin D researcher, the University of Toronto's Reinhold Vieth, says he has been knocking back 8,000 units a day - four times the maximum - for years.

Should everyone be doing the same?

Dr. Vieth says he believes that what he's doing is completely safe - after all, his intake is similar to the amount of vitamin D a sunbathing Canadian might make naturally on a summer day.

And Robert Heaney, a medical researcher at Creighton University in Omaha, says his Canadian colleague is hardly alone in his super-sized approach. "All the vitamin D researchers, to a person, I've not found an exception, are convinced enough by the data to walk the walk," says Dr. Heaney, who last year helped to conduct a study, reported in the *American Journal of Clinical Nutrition*, that linked vitamin D supplements to an astonishing 60-per-cent decrease in cancer incidence among middle-aged and older women.

Cedric Garland argues that, rather than pollutants or some other cause, insufficient levels of vitamin D are at the

root of the Western world's cancer epidemic. What's more, if more people took supplements, the population of northern regions would be a lot healthier all round.

"We will be preventing an extremely broad range of diseases in a single, inexpensive way with virtually no complications," he explains. "It will affect every branch of medicine and public health favourably."

TOO GOOD TO BE TRUE?

It seems almost inconceivable that geography could damn someone to a life-threatening illness - that the mere fact of living in a northern country such as Canada could be a health hazard.

The Garland brothers' hypothesis also defies the long-held conventional view that cancer is caused mainly by bad lifestyle habits, bad genes or carcinogens. Indeed, it suggests that some types of cancer could be better described as nutritional-deficiency diseases, much like scurvy or rickets.

Consequently, many experts have been skeptical, aware that much-touted nutrients in the past have often failed to live up to their initial hype.

"The problem with vitamins has been that generally the evidence, for whatever reason, doesn't pan out," cautions Len Lichtenfeld, deputy chief medical officer of the American Cancer Society.

Dr. Lichtenfeld says medical authorities have been burned so often over supplements that he would like to see a "substantial amount" of additional research before he is convinced that vitamin D is the real thing.

The idea that sunlight has beneficial health effects also flies in the face of advice to avoid sun exposure to reduce the risk of skin cancer.

Nevertheless, the idea that vitamin D insufficiency plays a role in cancer and other chronic adult diseases continues to gain scientific credence as a plausible theory, earned new respect for the long-underappreciated vitamin.

Though it first drew attention in the 1920s as a cure for rickets (bone health, not cancer, is why Health Canada even has a recommended intake), it has largely been treated like Rodney Dangerfield ever since. In our health-conscious age, it has been overshadowed by supplements such as vitamin C and beta carotene.

But since the Garland brothers kicked off interest in vitamin D with their data on colon cancer, other studies have shown that more than a dozen other cancers, including the big killers, breast and prostate, as well as an array of other diseases appear sensitive to insufficiencies of the vitamin.

The idea behind the research is simple: Humans evolved in a sunlight-filled environment near the equator, and still have countless biological processes exquisitely calibrated to the rich vitamin D levels we would have if we were still basking under the hot sun year-round.

But by migrating to higher latitudes, where strong sunlight is not present during the fall and winter, most humans upset their vitamin D metabolism, creating susceptibilities to chronic ailments that research is now linking to insufficiencies.

The question for Canadians is: If we're so short of a crucial vitamin, shouldn't we be compensating? And if we did, would vitamin D be a proverbial magic pill, capable of curing much of what ails us?

Although the guidelines jointly issued by the U.S. and Canadian governments say adults need only 200 to 600 IU of vitamin D daily, depending on age, the women in Dr. Heaney's study took 1,100 IU daily, while he himself takes 1,500 IU daily.

(Although the international units nomenclature makes the numbers seem large, the actual weight represented by a single IU of vitamin D is dust-like, at less than a millionth of a gram. The vitamin, by acting like a hormone in

the body's cells, packs a big biological punch in minute amounts.)

Radical conservatives

The Canadian Cancer Society is one of the more conservative health-advocacy agencies, but last year became the first major organization in the world to embrace the idea of large-scale, population-wide vitamin D supplementation to combat cancer. It started recommending that white adults take up to 1,000 IU daily in fall and winter, and non-whites, because of their higher susceptibility to vitamin D insufficiency at northern latitudes, take that amount year-round. (Canada doesn't keep national illness statistics by race, so the degree to which non-whites are being affected by ailments linked to low vitamin D levels isn't known.)

The Canadian Pediatric Society followed suit shortly after, calling for pregnant and breastfeeding women to take 2,000 IU daily, with a goal of preventing childhood diseases.

The Canadian Cancer Society's decision came after years of monitoring the research. Vitamin D "kept coming up. It kept hitting the bar that reaches your attention," says Heather Logan, the society's director of cancer-control policy.

"It wasn't one study and that was the end of the story. There were multiple research studies continued to be published in peer-reviewed journals."

One study, in the journal *Circulation*, found that those with low vitamin D status had a 62-per-cent increased risk of heart failure. Another, published in *Archives of Internal Medicine*, found that those who take vitamin D supplements cut mortality risk by 7 per cent. A third report, by scientists at the U.S. National Cancer Institute, found that, while vitamin D didn't affect overall cancer-death risk, those with relatively high levels of it in their blood had a 72-per-cent lower risk of dying from colorectal cancer.

Other studies have found that low blood levels are an excellent predictor of who goes on to develop cancer and heart disease and that people diagnosed with cancer during the vitamin D-rich summer have a better prognosis than those diagnosed during winter.

Not everyone is convinced, however. Critics charge that most of the findings - such as the Garlands' cancer maps - constitute only circumstantial evidence. And when the Canadian Cancer Society asked the American Cancer Society to join them in recommending more vitamin D, it refused.

"I think it's fair to say we had discussions and we agreed to disagree on that. Our position is that we really want what I call solid evidence ... that there in fact is a reduction in cancer mortality without a significant increase in risk with vitamin D supplementation," Dr. Lichtenfeld says. He wants to see drug-style clinical trials to validate the benefits and assess the risks, he says, before telling 330 million Americans to start taking supplements.

Similarly, John McLaughlin, vice-president of preventive oncology for Cancer Care Ontario, says the research on vitamin D is too thin at this point to recommend taking higher doses to prevent cancer. He dismisses Dr. Heaney's study as "largely uninformative" because of its small size (about 450 women) and because the subjects also took calcium supplements, which may have affected the results.

But even though Ms. Logan says the Canadian Cancer Society agrees that all the science on vitamin D may not be in yet, evidence to date strongly suggests that not acting on the implications of the research is risky. Cancers affected include such big killers as breast, prostate and colon, which will claim more than 10,000 Canadians this year.

"You don't need to wait for every scientific question to be answered before you take action," Ms. Logan says. "Where there is evidence of harm, even in the face of scientific uncertainty, you should do something about it."

Martin Mittelstaedt is The Globe and Mail's environment reporter.

JUST D FACTS: Vitamin D is measured by levels in blood. Many Canadians have 40 nanomoles/litre or less, particularly in winter. Many researchers believe levels need to be at least twice that high to reduce chronic disease risk.

Vitamin D is produced when exposed skin has a photochemical reaction to ultraviolet light rays from the sun. Nearly all the vitamin D circulating in our bodies is made this way, with a typical white-skinned person in a bathing suit under a noonday summer sun in Canada producing about 10,000 international units in 15 to 20 minutes. Non-whites need about five times longer to make the same amount, because the melanin in their skin acts as a sunscreen against UVB rays. During the fall and winter, sunlight at Canadian latitudes is too weak to cause any vitamin D production.

Vitamin D synthesis in skin occurs only when the UV index is three or higher, roughly the period around noon from March to October in southern parts of the country. A rule of thumb is that if your shadow is longer than you are, the sunlight is not intense enough.

Some of the very few foods that contain vitamin D are: cod liver oil (1,300 IU per tablespoon); wild salmon (1,000 IU per serving); farmed salmon (250 IU); sardines (600 IU); fortified milk or orange juice (100 IU); egg yolk (25 IU); fresh shiitake mushrooms and some organ meats (traces in both). Most multivitamins contain 400 IU. Over-the-counter pills and drops contain up to 1,000 IU.

Health Canada's daily intake recommendations, based primarily on a 1997 study, are: newborns to 12 months, 400 IU; age 1 to 50, 200 IU; 51 to 70, 400 IU; over 70, 600 IU; with an overall upper limit of 2,000 IU.

Many vitamin D advocates say Health Canada is too conservative. The Canadian Cancer Society, for example, recommends that non-white adults take 1,000 IU daily year-round and whites take that amount in fall and winter. The Canadian Pediatric Society recommends 2,000 IU daily for pregnant and breastfeeding women.

Toxicity has occurred after long-term exposure to massive amounts, ranging from 50,000 IU to 150,000 IU daily. Effects such as bone demineralization may occur with chronic daily doses exceeding 10,000 IU. No illnesses have been reported for doses under 3,800 IU daily.

A U.S. study in 2007 found that overall risk of cancer in women was cut by 60 per cent when they were given 1,100 IU of vitamin D per day, plus a calcium supplement.

Another study estimated the dose to cut colon-cancer risk in half: 1,000 IU daily. The amount estimated to cut breast-cancer risk in half: 4,000 IU daily. Researchers say women could stay within Health Canada guidelines and still reach 4,000 IU daily by getting 2,000 IU from diet and supplements and the rest from modest sun exposure.

There is some evidence that girls can cut their future risk of breast cancer by taking high levels of vitamin D during their teens.

U.S. researchers estimate that vitamin D insufficiency causes up to 60,000 premature cancer deaths a year in the country, or nearly 10 per cent of total mortality from the disease. If the same percentage applies to Canada, low vitamin D status leads to about 7,000 premature cancer deaths here annually.

While there is a risk of skin cancer from overexposure to ultraviolet light, researchers say, the benefits of modest sun exposure in preventing serious, hard-to-treat cancers outweighs that risk. Furthermore, they say, skin cancer is relatively easy to treat.

A 2001 Finnish study found that children given 2,000 IU daily cut their risk of getting juvenile diabetes by 80 per cent.

The strong correlation between latitude and the incidence of multiple sclerosis has led researchers to suspect the trend is related to vitamin D status. In the U.S., for example, MS rates are four times higher in northern states, along the Canadian border, than in the southern parts of the country. Similarly, Australian research shows the incidence of MS increases the farther people live from the equator. The highest incidence rates in the world are

found in Northern Europe and Canada.

Martin Mittelstaedt

GENE GENIE

New insights into how the 'magic pill' works

The role of vitamin D in carcinomas could explain one of the biggest mysteries about the cause of cancer: why so many people who develop the disease have no known risk factors, such as a family history of the illness.

The simple answer may be that Vitamin D interacts with an unusually large number of our genes, working like a master switch to turn them on or off. Researchers believe a deficiency of the vitamin leads to a deficiency of the proteins manufactured under the direction of these genes, which then undermines key defences against seemingly unrelated diseases such as cancer, diabetes and multiple sclerosis.

John White, who has been studying the antimicrobial activities of vitamin D at McGill University in Montreal, says that "virtually every cell" in the human body has receptors for vitamin D and that hundreds of different genes may be regulated by it.

Vitamin D's most profound gene-influenced activity appears to be in keeping healthy the broad category of cells known as epithelium, which line the outsides of our organs and the surfaces of the structures in our body.

Even though these lining tissues amount to only about 2 per cent of the weight of our bodies, they are the source of about 85 per cent of cancers, those known as carcinomas.

These include cancer of the colon, prostate, pancreas and uterus, along with the most common type of breast cancer, ductal carcinoma, which develops on milk-duct lining. (The other main type of cancer, sarcomas, appear in muscles and connective tissue, and don't have a strong association with vitamin D insufficiency.)

"Vitamin D is a particularly effective agent in inhibiting abnormal growth or development of malignancies in epithelial tissues," says Cedric Garland, a professor of preventive medicine at the University of California, San Diego.

Although many researchers view cancer as a hopelessly complex disease with different causes for each tumour type, Dr. Garland, who has been studying vitamin D for more than three decades, believes the carcinomas have a common origin in low levels of the vitamin. By his estimate, up to 75 per cent of these cancers could be prevented if vitamin D levels were raised through supplements. "I'm convinced that cancer is largely a vitamin D deficiency disease," he says.

One important function of vitamin D at the gene level that may explain its anti-cancer properties is that it helps to regulate the production of E-Cadherin, a type of biological glue that holds cells together. When this glue is in short supply, it allows epithelial cells to lose adhesion to one another, permitting some to escape from the tissue they are supposed to be embedded in. Unconstrained, these cells start to multiply at a greater rate than they otherwise would and begin forming the lesions that ultimately turn into cancers.

Vitamin D plays a role in telling cells when to die, thus helping to prevent uncontrolled proliferation and curbing the growth of new blood vessels that nourish growing tumours.

It may also play a role in diseases unrelated to cancer. A main biological function of epithelial cells is to be a barrier against viruses and bacteria that cause infections.

Scientists speculate that when low vitamin D status weakens epithelial cells, the barrier function is compromised, exposing tissues to attack from disease-causing agents - in diabetes, for example, by weakening islet cells; in multiple sclerosis, by weakening glial cells in the nervous system; and in tuberculosis, by reducing the ability of the lung lining to repulse bacteria, according to Dr. Garland.

Some medical researchers have even begun to suspect a link between vitamin D insufficiency and schizophrenia, which occurs 10 per cent more often among those born in winter and early spring, when vitamin D from sunshine is less available.

Researchers in Australia are testing this hypothesis by studying the brains of rats born to pregnant mothers deprived of vitamin D - with alarming results. The vitamin-D-deprived rodent brains had more cell proliferation, enlarged ventricles and less of a protein necessary for nerve growth.

"What we see is that when you take [vitamin] D out of the brain in the rodent, you can break their brain basically," says John McGrath, a professor at the Queensland Brain Institute at the University of Queensland in Brisbane. "We can change the way their brain develops."

Dr. McGrath says it is too early to say whether the rodent-brain research applies to humans. But he adds that "even if only a small fraction of [the cases of] schizophrenia could be averted by optimizing maternal nutrition, that is going to be a really important outcome."

Martin Mittelstaedt (original article ----->)

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