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REPORT

Unraveling a Centuries-Old Mystery

Why Is Flu Risk So Much Higher in the Winter?

By Dale Kiefer



This age-old mystery has confounded scientists for the last century. Like clockwork, influenza infects the majority of its victims during the winter months in both the Northern and Southern hemispheres. Infection with the flu virus leaves millions around the world bedridden with debilitating symptoms such as fever, body pains, sore throat, and cough. The very young and elderly are particularly susceptible to catastrophic complications from the flu, including death. Moreover, the recent emergence of flu strains such as H5N1 leaves many experts on infectious disease worried about the potential for global devastation even worse than that of the 1918-19 flu pandemic, which was linked to at least 50 million deaths worldwide.

A fascinating new theory seeks to explain why flu takes hold during the winter months and why it infects so many people, particularly elderly adults. At the heart of this theory is the presence of a vitamin deficiency in certain populations, including aging adults, around the world.

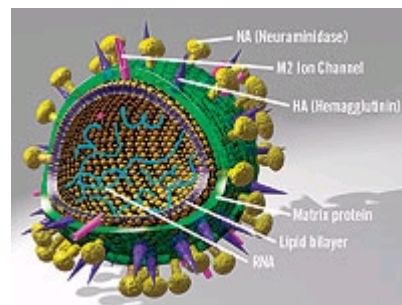
In this article, we examine this intriguing theory, and how defending against the flu may be as simple as taking enough of a common **nutritional supplement**.

INFLUENZA OUTBREAK: A MODERN MYSTERY

One of the greatest medical mysteries of the ages may finally have been solved, thanks to a newly published theory regarding the relationship between influenza and its peak onset during the winter months.¹ Published just months before the start of the annual flu season, this novel theory addresses questions that have puzzled scientists for decades: why does flu strike almost exclusively in winter, and why are the elderly often at greatest risk of contracting the disease?

The answers to these questions are of more than academic interest. In the US alone, influenza hospitalizes more than 100,000 people—and kills more than 30,000—in an average year.^{2,3} With the recent scares over avian (bird) flu and severe acute respiratory syndrome (SARS), many scientists believe it is only a matter of time before the world is gripped by a deadly pandemic. Improving our understanding of these diseases may help us avert disaster from influenza and other severe respiratory viruses.

Surprisingly, the solution may be as simple as supplementing with higher-than-usual amounts of a common vitamin in the fall and winter months.^{2,4} The story behind this proactive approach to flu prevention begins in England more than a quarter century ago, eventually coming to fruition in California.



Avian Flu Virus (H5N1)

POPULAR MISCONCEPTIONS ABOUT THE FLU

First, some background on the influenza virus is in order. Epidemiological data from around the globe indicate that while flu cases are not entirely unheard of in summer, outbreaks of this virus peak soon after the winter solstice in temperate latitudes.⁵ For years, health experts have speculated that the explanation for this seasonality is that people tend to congregate indoors more often in winter, thus fostering rapid person-to-person transmission. However, in this age of ubiquitous air conditioning and 9-to-5 jobs, is there really much difference in the potential for interpersonal contact from one season to another? While children probably spend more time indoors in winter due to school schedules, what about adults?

In fact, the “huddling inside” explanation has never been found to account for the seasonal nature of influenza infection. In a recent article on influenza transmission, a respected researcher at the federal Centers for Disease Control and Prevention noted that no human experimental studies have delineated the person-to-person transmission of influenza. Instead, the virus appears to

be spread through indirect contact, with transmission through respiratory droplets the most probable explanation at this time.⁵ However, since these minute respiratory particles are unavoidable, this theory fails to explain why influenza occurs more often in winter and why certain individuals demonstrate protection against the flu. This puzzle has led researchers to continue searching for factors contributing to the infectious nature of influenza viruses.

UNRAVELING THE INFLUENZA-WINTER SEASON CONNECTION

Dr. John Cannell, a California psychiatrist, is the chief author of a landmark theory that postulates that influenza epidemics are intimately linked to declining vitamin D levels.¹

In California, Dr. Cannell works with patients at a maximum-security hospital for the criminally insane. In recent years, he had become aware that vitamin D is a unique compound with profound effects on human immunity. He had kept abreast of cutting-edge research demonstrating that vitamin D has numerous wide-ranging effects in the body, influencing everything from bone health and cancer prevention to blood pressure.^{1,6,7} Dr. Cannell also knew that an alarming number of otherwise healthy people are deficient in this crucial vitamin, especially in winter. "I realized that vitamin D is really quite different from other vitamins," he recently told Life Extension.

Most of Dr. Cannell's patients are African-Americans whose skin pigmentation interferes with the sunlight-driven production of natural vitamin D. This fact, combined with their confinement, led Dr. Cannell to suspect that his patients' blood levels of vitamin D would be abnormally low. Testing confirmed this to be the case. After educating his patients about vitamin D's potential benefits, Dr. Cannell prescribed routine supplementation with 2000 IU of vitamin D3 (cholecalciferol) daily. He says he would have given the men even higher doses, but 2000 IU represents the current "upper limit" of vitamin D intake recommended by the government-sponsored Food and Nutrition Board of the Institute of Medicine. By contrast, most adult multivitamins deliver just 400 IU of vitamin D, and a single eight-ounce glass of fortified milk delivers just 100 IU.⁷

PATIENTS STAY FLU-FREE AMIDST AN EPIDEMIC

In the late winter of 2005, influenza broke out at the hospital. Ward after ward was quarantined, as patients were gripped with the chills, fever, cough, and severe body aches characteristic of the influenza A strain of the virus. "First, the ward below mine was infected," says Dr. Cannell, "and then the wards on my right, left, and across the hall." To his growing amazement, however, his own patients remained unaffected. "My patients had intermingled with patients from infected wards before the quarantines," he notes. "I felt certain that my patients had been exposed to the influenza virus." His patients' enduring health in the midst of a local epidemic profoundly influenced Dr. Cannell's thoughts on the relationship between vitamin D and immunity to the flu.⁷



He recalled the work of a pioneering British physician, Dr. R. Edward Hope-Simpson. Working in virtual obscurity, Hope-Simpson was catapulted to fame in the mid-1960s when he discovered the cause of shingles, a painful condition that affects adults. Thanks to Hope-Simpson, we now know that shingles results from the reactivation of latent chicken pox virus. After announcing this widely hailed discovery, Hope-Simpson turned his attention to influenza and was the first to document that in temperate latitudes, influenza A epidemics invariably peak in the month following the winter solstice. This pattern holds true for both the Northern and Southern hemispheres, and cases tend to rise and fall for about two months before and after the peak.⁸

Noting the obvious relationship between the decline in sunshine and rise of influenza, Hope-Simpson proposed that an undetermined "seasonal stimulus" must be responsible. Although he recognized that solar radiation had to be involved in evoking this seasonal stimulus, he was at a loss as to what the actual stimulus might be. Before his death in 2003, Hope-Simpson published numerous papers documenting the seasonal nature of influenza. While flu cases occasionally occur in summer, they rarely cause communal outbreaks. It may seem like common sense to acknowledge that flu is a winter phenomenon, but the fact had never been scientifically documented before. Hope-Simpson also noted, and other scientists have now confirmed, that flu outbreaks in the tropics tend to occur in the rainy season, when sunshine is scarce.^{4,7,9}

VITAMIN D AND IMMUNITY: WHAT YOU NEED TO KNOW

- An intriguing new theory suggests that diminished winter blood levels of vitamin D increase people's susceptibility to influenza infection. Patients supplemented with vitamin D were shown to be completely protected against influenza infection, even while living in close proximity to people infected with flu.
- Vitamin D has far-ranging effects on the immune system. Dangerous flu virus strains stimulate white blood cells to produce inflammatory cytokines associated with severe illness, while vitamin D protects against this effect. Vitamin D enhances the production of antimicrobial peptides, which are proteins that protect organisms from infection-causing microbes such as viruses. Vitamin D also activates essential infection-fighting immune cells known as macrophages.
- People who live at higher latitudes, where less vitamin D is available from exposure to sunlight, experience a greater risk of illnesses such as multiple sclerosis, diabetes, osteoporosis, and certain cancers.
- People seeking to optimize immune health and protect against viral flu infections, particularly elderly adults, should consider supplementing with high-dose vitamin D, especially during the winter months.



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CHALLENGING POPULAR ASSUMPTIONS ABOUT INFLUENZA

Hope-Simpson questioned other beliefs about the nature of influenza. "Epidemics of influenza often occur contemporaneously at the same latitude, even in localities widely separated by longitude," he noted.⁸ But if outbreaks occur simultaneously in widely separated areas, how can person-to-person transmission be responsible?

Much has been made of the potential dangers of quickly transmitted infection, due to modern modes of transportation. However, through careful examination of ancient records, Hope-Simpson showed that virtually simultaneous outbreaks occurred in England long before the advent of modern roads, let alone continent-spanning jet-liners. This challenged the fundamental assumption that influenza is transmitted in a chain from one patient to another. Could it be that the flu virus lies dormant in a range of potential hosts, until some "seasonal stimulus" promotes its infectivity among these unwitting carriers?

Back in California, Dr. Cannell could not help but wonder whether vitamin D played a role in his patients' evident immunity to the flu. He knew several things that Hope-Simpson did not. For one, scientists now know that influenza infection prompts white blood cells known as macrophages to release immune system chemicals called cytokines and chemokines, which promote inflammation. Furthermore, scientists now know that the virus responsible for 1918's devastating global influenza pandemic was especially effective in stimulating the release of cytokines by macrophages.¹⁰ In fact, the severity of the resulting illness is believed to be proportional to a flu virus's ability to evoke cytokine production. In bird flu, for instance, this response can be overwhelming, resulting in death.^{11,12} Dr. Cannell also knew that research has recently shown that vitamin D modulates macrophages' production of chemokines and cytokines, in effect preventing them from overreacting to infectious stimuli and causing serious manifestations of viral infection.^{13,14}

VITAMIN D'S ROLE IN BOLSTERING IMMUNITY

Nor did Hope-Simpson have knowledge of another recently reported phenomenon. In the past few years, several independent researchers have shown that vitamin D significantly enhances the genetic expression of antimicrobial peptides in human monocytes (precursors to macrophages), neutrophils, and other immune system cells.^{15,16} These antimicrobial proteins help to destroy invading infectious microbes. With their broad-spectrum activity, they are capable of killing everything from bacteria to viruses. They have been shown to be an important part of the respiratory tract's defense against invaders, and likewise show promise in fighting the influenza virus.¹⁷⁻¹⁹



For Dr. Cannell, these various clues led to one inescapable conclusion: vitamin D—which is produced when the skin is exposed to summer sunlight, and which, conversely, declines in winter—plays a critical role in our vulnerability to influenza infection. In fact, vitamin D must surely be Hope-Simpson's mysterious "seasonal stimulus." Dr. Cannell consulted a number of leading vitamin D researchers, all of whom agreed with his conclusions. They include researchers from such venerable institutions as the National Institutes of Health and the Harvard School of Public Health. One of these scientists, Dr. Michael F. Holick, has been studying vitamin D for three decades.^{1,7,20}

In an interview with *Life Extension*, Dr. Holick alluded to the special relationship between vitamin D and the body's primary immune system defenders, the macrophages. "What intrigues me the most," Dr. Holick noted, "is that we've always known that macrophages activate vitamin D." The form of vitamin D generated through the skin's interaction with ultraviolet B radiation (from sunshine or artificial sources) is a pre-hormone. It must be converted in the body to its active hormone form, called 1,25-dihydroxyvitamin D3. An intermediary form, known as 25-hydroxyvitamin D, is the major circulating form of vitamin D, and is measured to determine vitamin D status.²⁰

VITAMIN D'S FAR-RANGING EFFECTS ON DISEASE PREVENTION

Most of this activation of vitamin D occurs in the liver and kidneys. However, the fact that macrophages facilitate the conversion of circulating vitamin D to its active form,²⁰ and that activated vitamin D in turn regulates the activity of macrophages, suggests an

important relationship between the two.

Dr. Holick notes that vitamin D receptors have been identified in virtually every cell in the body. "It's one of the earliest vitamins," he says. "It was made by phytoplankton (microscopic aquatic plants such as algae) 750 million years ago." He believes that vitamin D plays an important role in many aspects of health. "If you live at higher latitudes where less vitamin D is available from sunshine, you're more likely to suffer from diabetes, multiple sclerosis, and colon, breast, prostate, and pancreatic cancers," he says. "Even hypertension is associated with latitude. Patients exposed to sunlight increase their vitamin D levels, and their blood pressure comes down."

VITAMIN D DOSAGE SUGGESTIONS

- While the US recommended dietary allowance (RDA) for vitamin D is 400 IU per day,²⁵ many health authorities now recommend consuming 800 IU or more of vitamin D daily.²⁶
- Research suggests that the elderly in particular may benefit from higher vitamin D doses such as 2000 IU daily—and perhaps even up to 5000 IU daily—for optimal effects. Studies suggest that a healthy serum level of vitamin D (25-hydroxyvitamin D) is 75-125 nmol/L.²⁷
- Research published since 1997 suggests that vitamin D toxicity is very unlikely in healthy individuals at intake levels lower than 10,000 IU/day.²⁸⁻³⁰ Any individual taking high doses of vitamin D should be monitored for signs and symptoms of vitamin D toxicity.
- Vitamin D toxicity can cause symptoms such as nausea, vomiting, poor appetite, constipation, and weakness, and signs that include heart arrhythmias, kidney stones, and elevated blood levels of cholesterol, calcium, or liver enzymes.^{25,26}
- Vitamin D is contraindicated in individuals with hypercalcemia (high blood calcium levels).^{25,26}
- People with kidney disease and those who use digoxin or other cardiac glycoside drugs should consult a physician before using supplemental vitamin D. ^{25,26}

Dr. Holick has published numerous papers detailing the relationship between inadequate vitamin D levels and increased risk of diseases ranging from osteoporosis and arthritis to cardiovascular disease and cancers.^{21,22} "Activated vitamin D is one of the most potent inhibitors of cell growth," he notes, a fact that may explain its importance in cancer prevention. "I don't see any downside to taking pharmaceutical levels of vitamin D to fight prostate cancer," he adds.

THE IMPORTANCE OF VITAMIN D SUPPLEMENTS

The bottom line is that far too many people are deficient in vitamin D,^{22,23} especially the elderly.²⁴ Unfortunately, by following well-intentioned advice to minimize their exposure to the sun, aging adults may greatly diminish their ability to manufacture optimal levels of vitamin D, particularly compared to young people. This could put them at increased risk of contracting the flu.

Although Dr. Holick serves on the board responsible for amending existing government recommendations for vitamin D intake, he thinks it will be at least another four years before the government publishes new recommendations aimed at increasing vitamin D intake to adequate levels. According to Dr. Holick, there is simply too much data being generated too quickly, by researchers around the world, for committee members to evaluate it any faster.

Nevertheless, he strongly advises aging adults to begin increasing their supplemental intake of vitamin D now, especially in winter, when sunlight exposure at higher latitudes is insufficient to produce adequate vitamin D levels naturally. "Most people should supplement with vitamin D," says Dr. Holick. "It's perfectly safe to take, and is likely to have a benefit for all aspects of health."

Dr. Holick anticipates that if enough people get the message, we are likely to see a noticeable drop in everything from cancer cases to flu outbreaks. "It would be quite amazing," he says. "It might very well markedly decrease a person's risk." Dr. Holick himself takes 1000 IU of vitamin D every day.

Dr. Cannell's approach to vitamin D for disease prevention is even more aggressive. He and his family members take 5000 IU of supplemental vitamin D daily during the winter months. "The implications are breathtaking," says Dr. Cannell. "The best thing may be not to stock up on antiviral drugs, but to get some sunshine. Should you go into the flu season vitamin D deficient? No. It's a widespread problem, and it should be addressed."



The intriguing theory that vitamin D may help prevent or arrest viral respiratory infections has tremendous potential in helping million of people avert these potentially deadly outbreaks. To date, however, no interventional studies in humans have been conducted. Such trials are sorely needed to assess vitamin D's efficacy in preventing or treating influenza.

In the meantime, however, all health-conscious people would be well advised to optimize their daily intake of vitamin D, particularly during the winter months. This low-cost dietary supplement may just be the best possible medicine for guarding against the flu virus and bolstering your protection against a host of age-related afflictions.

ARE YOU VITAMIN D DEFICIENT?

Most people think they get enough vitamin D from sun exposure and dietary sources such as milk.

In fact, many people actively avoid the sun or use sunscreen to reduce their risk of skin cancer. Aging adults and those with impaired mobility due to chronic disease may become more homebound and not get out in the sun as much. In much of the northern US, available sunshine is inadequate to stimulate enough vitamin D formation in the winter. And while fatty fish, such as salmon and mackerel, contain large amounts of vitamin D, and milk is fortified with vitamin D, most foods contain very little vitamin D. As a result, the prevalence of vitamin D deficiency in the US has been reported to be as high as 21-58% in adolescents and adults,³¹ and 54% in homebound older adults.³²

Those who take vitamin D supplements are sometimes lulled into a false sense of security that they have adequate levels of vitamin D in their bodies. To the surprise of doctors who are testing their patients' blood for vitamin D, there are some people who require more than 5000 IU/day of supplemental vitamin D to achieve optimal blood levels.

For these reasons, it makes sense to assess your vitamin D status. Life Extension now offers a simple blood test that can help you detect vitamin D deficiency. Optimizing your vitamin D intake provides vital immune support that can help you guard against the influenza virus and a host of age-related diseases.

Ideal blood (serum) levels of vitamin D are 75-125 nmol/L. A vitamin D blood test costs members \$47. When having your blood tested for vitamin D, you may also consider obtaining a CBC/Chemistry Blood Test for only \$35. This comprehensive panel provides measurements of kidney function and blood calcium levels, in addition to cholesterol, LDL, HDL, triglycerides, glucose, and a host of other important factors that you should know about. The Vitamin D and CBC Chemistry blood tests can be ordered by calling 1-800-208-3444.

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