

Epidemic Influenza And Vitamin D

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In early April of 2005, after a particularly rainy spring, an influenza epidemic (epi: upon, demic: people) exploded through the maximum-security hospital for the criminally insane where I have worked for the last ten years. It was not the pandemic (pan: all, demic: people) we all fear, just an epidemic. The world is waiting and governments are preparing for the next pandemic. A severe influenza pandemic will kill many more Americans than died in the World Trade Centers, the Iraq war, the Vietnam War, and Hurricane Katrina combined, perhaps a million people in the USA alone. Such a disaster would tear the fabric of American society. Our entire country might resemble the Superdome or Bourbon Street after Hurricane Katrina.

It's only a question of when a pandemic will come, not if it will come. Influenza A pandemics come every 30 years or so, severe ones every hundred years or so. The last pandemic, the Hong Kong flu, occurred in 1968 - killing 34,000 Americans. In 1918, the Great Flu Epidemic killed more than 500,000 Americans. So many millions died in other countries, they couldn't bury the bodies. Young healthy adults, in the prime of their lives in the morning, drowning in their own inflammation by noon, grossly discolored by sunset, were dead at midnight. Their body's own broad-spectrum natural antibiotics, called antimicrobial peptides, seemed nowhere to be found. An overwhelming immune response to the influenza virus - white blood cells releasing large amounts of inflammatory agents called cytokines and chemokines into the lungs of the doomed - resulted in millions of deaths in 1918.

As I am now a psychiatrist, and no longer a general practitioner, I was not directly involved in fighting the influenza epidemic in our hospital. However, our internal medicine specialists worked overtime as they diagnosed and treated a rapidly increasing number of stricken patients. Our Chief Medical Officer quarantined one ward after another as more and more patients were gripped with the chills, fever, cough, and severe body aches that typifies the clinical presentation of influenza A.

Epidemic influenza kills a million people in the world every year by causing pneumonia, "the captain of the men of death." These epidemics are often explosive; the word influenza comes from Italian (Medieval Latin ?nfluentia) or influence, because of the belief that the sudden and abrupt epidemics were due to the influence of some extraterrestrial force. One seventeenth century observer described it well when he wrote, "suddenly a Distemper arose, as if sent by some blast from the stars, which laid hold on very many together: that in some towns, in the space of a week, above a thousand people fell sick together."

I guess our hospital was under luckier stars as only about 12% of our patients were infected and no one died. However, as the epidemic progressed, I noticed something unusual. First, the ward below mine was infected, and then the ward on my right, left, and across the hall - but no patients on my ward became ill. My patients had intermingled with patients from infected wards before the quarantines. The nurses on my unit cross-covered on infected wards. Surely, my patients were exposed to the influenza A virus. How did my patients escape infection from what some think is the most infectious of all the respiratory viruses?

My patients were no younger, no healthier, and in no obvious way different from patients on other wards. Like other wards, my patients are mostly African Americans who came from the same prisons and jails as patients on the infected wards. They were prescribed a similar assortment of powerful psychotropic medications we use throughout the hospital to reduce the symptoms of psychosis, depression, and violent mood swings and to try to prevent patients from killing themselves or attacking other patients and the nursing staff. If my patients were similar to the patients on all the adjoining wards, why didn't even one of my patients catch the flu?

A short while later, a group of scientists from UCLA published a remarkable paper in the prestigious journal, Nature. The UCLA group confirmed two other recent studies, showing that a naturally occurring steroid hormone - a hormone most of us take for granted - was, in effect, a potent antibiotic. Instead of directly killing bacteria and viruses, the steroid hormone under question increases the body's production of a remarkable class of proteins, called antimicrobial peptides. The 200 known antimicrobial peptides directly and rapidly destroy the cell walls of bacteria, fungi, and viruses, including the influenza virus, and play a key role in keeping the lungs free of infection. The steroid hormone that showed these remarkable antibiotic properties was plain old vitamin D.

All of the patients on my ward had been taking 2,000 units of vitamin D every day for several months or longer. Could that be the reason none of my patients caught the flu? I then contacted Professors Reinhold Vieth and Ed Giovannucci and told them of my observations. They immediately advised me to collect data from all the patients in the hospital on 2,000 units of vitamin D, not just the ones on my ward, to see if the results were statistically significant. It turns out that the observations on my ward alone were of borderline statistical significance and could have been due to chance alone. Administrators at our hospital agreed, and are still attempting to collect data from all the patients in the hospital on 2,000 or more units of vitamin D at the time of the epidemic.

Four years ago, I became convinced that vitamin D was unique in the vitamin world by virtue of three facts. First, it's the only known precursor of a potent steroid hormone, calcitriol, or activated vitamin D. Most other vitamins are antioxidants or co-factors in enzyme reactions. Activated vitamin D - like all steroid hormones - damasks the genome, turning protein production on and off, as your body requires. That is, vitamin D regulates genetic expression in hundreds of tissues throughout your body. This means it has as many potential mechanisms of action as genes it damasks.

Second, vitamin D does not exist in appreciable quantities in normal human diets. True, you can get several thousand units in a day if you feast on sardines for breakfast, herring for lunch and salmon for dinner. The only people who ever regularly consumed that much fish are peoples, like the Inuit, who live at the extremes of latitude. The milk Americans depend on for their vitamin D contains no naturally occurring vitamin D; instead, the U.S. government requires fortified milk to be supplemented with vitamin D, but only with what we now know to be a paltry 100 units per eight-ounce glass.

The vitamin D steroid hormone system has always had its origins in the skin, not in the mouth. Until quite recently, when dermatologists and governments began warning us about the dangers of sunlight, humans made enormous quantities of vitamin D where humans have always made it, where naked skin meets the ultraviolet B radiation of sunlight. We just cannot get adequate amounts of vitamin D from our diet. If we don't expose ourselves to ultraviolet light, we must get vitamin D from dietary supplements.

The third way vitamin D is different from other vitamins is the dramatic difference between natural vitamin D nutrition and the modern one. Today, most humans only make about a thousand units of vitamin D a day from sun exposure; many people, such as the elderly or African Americans, make much less than that. How much did humans normally make? A single, twenty-minute, full body exposure to summer sun will trigger the delivery of 20,000 units of vitamin D into the circulation of most people within 48 hours. Twenty thousand units, that's the single most important fact about vitamin D. Compare that to the 100 units you get from a glass of milk, or the several hundred daily units the U.S. government recommend as "Adequate Intake." It's what we call an "order of magnitude" difference.

Humans evolved naked in sub-equatorial Africa, where the sun shines directly overhead much of the year and where our species must have obtained tens of thousands of units of vitamin D every day, in spite of our skin developing heavy melanin concentrations (racial pigmentation) for protecting the deeper layers of the skin. Even after humans migrated to temperate latitudes, where our skin rapidly lightened to allow for more rapid vitamin D production, humans worked outdoors. However, in the last three hundred years, we began to work indoors; in the last one hundred years, we began to travel inside cars; in the last several decades, we began to lather on sunblock and consciously avoid sunlight. All of these things lower vitamin D blood levels. The inescapable conclusion is that vitamin D levels in modern humans are not just low - they are aberrantly low.

About three years ago, after studying all I could about vitamin D, I began testing my patient's vitamin D blood levels and giving them literature on vitamin D deficiency. All their blood levels were low, which is not surprising as vitamin D deficiency is practically universal among dark-skinned people who live at temperate latitudes. Furthermore, my patients come directly from prison or jail, where they get little opportunity for sun exposure. After finding out that all my patients had low levels, many profoundly low, I started educating them and offering to prescribe them 2,000 units of vitamin D a day, the U.S. government's "Upper Limit."

Could vitamin D be the reason none of my patients got the flu? In the last several years, dozens of medical studies have called attention to worldwide vitamin D deficiency, especially among African Americans and the elderly, the two groups most likely to die from influenza. Cancer, heart disease, stroke, autoimmune disease, depression, chronic pain, depression, gum disease, diabetes, hypertension, and a number of other diseases have recently been associated with vitamin D deficiency. Was it possible that influenza was as well?

Then I thought of three mysteries that I first learned in medical school at the University of North Carolina: (1) although the influenza virus exists in the population year-round, influenza is a wintertime

illnesses; (2) children with vitamin D deficient rickets are much more likely to suffer from respiratory infections; (3) the elderly in most countries are much more likely to die in the winter than the summer (excess wintertime mortality), and most of that excess mortality, although listed as cardiac, is, in fact, due to influenza.

Could vitamin D explain these three mysteries, mysteries that account for hundreds of thousands of deaths every year? Studies have found the influenza virus is present in the population year-around; why is it a wintertime illness? Even the common cold got its name because it is common in cold weather and rare in the summer. Vitamin D blood levels are at their highest in the summer but reach their lowest levels during the flu and cold season. Could such a simple explanation explain these mysteries?

The British researcher, Dr. R. Edgar Hope-Simpson, was the first to document the most mysterious feature of epidemic influenza, its wintertime surfeit and summertime scarcity. He theorized that an unknown "seasonal factor" was at work, a factor that might be affecting innate human immunity. Hope-Simpson was a general practitioner who became famous in the late 1960's after he discovered the cause of shingles. British authorities bestowed every prize they had on him, not only because of the importance of his discovery, but because he made the discovery own his own, without the benefit of a university appointment, and without any formal training in epidemiology (the detective branch of medicine that methodically searches for clues about the cause of disease).

After his work on shingles, Hope-Simpson spent the rest of his working life studying influenza. He concluded a "seasonal factor" was at work, something that was regularly and predictably impairing human immunity in the winter and restoring it in the summer. He discovered that communities widely separated by longitude, but which shared similar latitude, would simultaneously develop influenza. He discovered that influenza epidemics in Great Britain in the 17th and 18th century occurred simultaneously in widely separated communities, before modern transportation could possibly explain its rapid dissemination. Hope-Simpson concluded a "seasonal factor" was triggering these epidemics. Whatever it was, he was certain that the deadly "crop" of influenza that sprouts around the winter solstice was intimately involved with solar radiation. Hope-Simpson predicted that, once discovered, the "seasonal factor" would "provide the key to understanding most of the influenza problems confronting us."

Hope-Simpson had no way of knowing that vitamin D has profound effects on human immunity, no way of knowing that it increases production of broad-spectrum antimicrobial peptides, peptides that quickly destroy the influenza virus. We have only recently learned how vitamin D increases production of antimicrobial peptides while simultaneously preventing the immune system from releasing too many inflammatory cells, called chemokines and cytokines, into infected lung tissue.

In 1918, when medical scientists did autopsies on some of the fifty million people who died during the 1918 flu pandemic, they were amazed to find destroyed respiratory tracts; sometimes these inflammatory cytokines had triggered the complete destruction of the normal epithelial cells lining the respiratory tract. It was as if the flu victims had been attacked and killed by their own immune systems. This is the severe inflammatory reaction that vitamin D has recently been found to prevent.

I subsequently did what physicians have done for centuries. I experimented, first on myself and then on my family, trying different doses of vitamin D to see if it has any effects on viral respiratory infections. After that, as the word spread, several of my medical colleagues experimented on themselves by taking three-day courses of pharmacological doses (2,000 units per kilogram per day) of vitamin D at the first sign of the flu. I also asked numerous colleagues and friends who were taking physiological doses of vitamin D (5,000 units per day in the winter and less, or none, in the summer) if they ever got colds or the flu, and, if so, how severe the infections were. I became convinced that physiological doses of vitamin D reduce the incidence of viral respiratory infections and that pharmacological doses significantly ameliorate the symptoms of some viral respiratory infections if taken early in the course of the illness. However, such observations are so personal, so likely to be biased, that they are worthless science.

As I waited for the hospital to finish collecting data from all the patients taking vitamin D at the time of the outbreak - to see if it really reduced the incidence of influenza - I decided to research the literature thoroughly, finding all the clues in the world's medical literature that indicated if vitamin D played any role in preventing influenza or other viral respiratory infections. I worked on the paper for over a year, writing it with Professor Edward Giovannucci of Harvard, Professor Reinhold Vieth of the University of Toronto, Professor Michael Holick of Boston University, Professor Cedric Garland of U.C., San Diego, as well as Dr. John Umhau of the National Institute of Health, Sasha Madronich of the National Center for Atmospheric Research, and Dr. Bill Grant at the Sunlight, Nutrition and Health Research Center. After numerous revisions, we submitted our paper to the same widely respected journal where Dr. Hope-Simpson published most of his work several decades ago.

Epidemiology and Infection, known as *The Journal of Hygiene* in Hope-Simpson's day, recently published our [paper](#). The editor, Professor Norman Noah, knew Dr. Hope-Simpson and helped tremendously with the paper. In the paper, we detailed our theory that vitamin D is Hope-Simpson's long forgotten "seasonal stimulus." We proposed that annual fluctuations in vitamin D levels explain the seasonality of influenza. The periodic seasonal fluctuations in 25-hydroxy-vitamin D levels, which cause recurrent and predictable wintertime vitamin D deficiency, predispose human populations to influenza epidemics. We raised the possibility that influenza is a symptom of vitamin D deficiency in the same way that an unusual form of pneumonia (*pneumocystis carinii*) is a symptom of AIDS. That is, we theorized that George Bernard Shaw was right when he said, "the characteristic microbe of a disease might be a symptom instead of a cause."

In the paper, we propose that vitamin D explains the following 14 observations:

1. Why the flu predictably occurs in the months following the winter solstice, when vitamin D levels are at their lowest,
2. Why it disappears in the months following the summer solstice,
3. Why influenza is more common in the tropics during the rainy season,
4. Why the cold and rainy weather associated with El Nino Southern Oscillation (ENSO), which drives people indoors and lowers vitamin D blood levels, is associated with influenza,
5. Why the incidence of influenza is inversely correlated with outdoor temperatures,
6. Why children exposed to sunlight are less likely to get colds,
7. Why cod liver oil (which contains vitamin D) reduces the incidence of viral respiratory infections,
8. Why Russian scientists found that vitamin D-producing UVB lamps reduced colds and flu in schoolchildren and factory workers,
9. Why Russian scientists found that volunteers, deliberately infected with a weakened flu virus - first in the summer and then again in the winter - show significantly different clinical courses in the different seasons,
10. Why the elderly who live in countries with high vitamin D consumption, like Norway, are less likely to die in the winter,
11. Why children with vitamin D deficiency and rickets suffer from frequent respiratory infections,
12. Why an observant physician (Rehman), who gave high doses of vitamin D to children who were constantly sick from colds and the flu, found the treated children were suddenly free from infection,
13. Why the elderly are so much more likely to die from heart attacks in the winter rather than in the summer,
14. Why African Americans, with their low vitamin D blood levels, are more likely to die from influenza and pneumonia than Whites are.

Although our paper discusses the possibility that physiological doses of vitamin D (5,000 units a day) may prevent colds and the flu, and that physicians might find pharmacological doses of vitamin D (2,000 units per kilogram of body weight per day for three days) useful in treating some of the one million people who die in the world every year from influenza, we remind readers that it is only a theory. Like all theories, our theory must withstand attempts to be disproved with dispassionately conducted and well-controlled scientific experiments.

However, as vitamin D deficiency has repeatedly been associated with many of the diseases of civilization, we point out that it is not too early for physicians to aggressively diagnose and adequately treat vitamin D deficiency. We recommend that enough vitamin D be taken daily to maintain 25-hydroxy vitamin D levels at levels normally achieved through summertime sun exposure (50 ng/ml). For many persons, such as African Americans and the elderly, this will require up to 5,000 units daily in the winter and less, or none, in the summer, depending on summertime sun exposure.

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