Low Vitamin D Seen as Factor in Tuberculosis

BY BRUCE JANCIN
Denver Bureau

KYOTO, JAPAN — The rationale for proposed clinical trials of vitamin D supplementation as adjunctive therapy in tuberculosis—and perhaps in a wide-ranging assortment of other diseases—has origins stretching as far back as the tuberculosis sanatorium movement that originated in Germany during the 1800s, according to Dr. Robert L. Modlin.

Another relevant milestone was the 1903 Nobel Prize in medicine or physiology awarded to Dr. Niels Ryberg Finsen of Denmark for demonstrating the therapeutic benefit of concentrated UV light in patients with cutaneous tuberculosis, also known as lupus vulgaris, Dr. Modlin added at an international investigative dermatology meeting.

Dr. Finsen didn't really understand the mechanism of benefit provided by his UV-generating "Finsen boxes," nor did proponents of the sanitorium movement know why exposing tuberculosis patients to fresh mountain summer air and sunlight caused them to get better, said Dr. Modlin, professor and chief of dermatology, and professor of microbiology, immunology, and molecular genetics at the University of California, Los Angeles.

The association between reduced vitamin D status and increased susceptibility to tuberculosis wasn't recognized until decades later.

And it was later still—in fact, only a couple of years ago—that Dr. Modlin and his coworkers demonstrated in a landmark study the detailed physiologic mechanism by which vitamin D exerts antimicrobial effects in the skin (Science 2006;311:1770-3).

This study established vitamin D as the key link between macrophage activation by toll-like receptors and the downstream antimicrobial responses of the innate immune system that help fight off bacterial infection. The research provided a mechanistic explanation for the known association between low serum vitamin D and tuberculosis.

How might these findings eventually translate into clinical care? Dr. Modlin noted that African Americans, for example, have a high prevalence of low serum vitamin D and are also more susceptible than other Americans to tuberculosis. This raises the possibility that vitamin D supplementation might be an inexpensive and safe preventive intervention aimed at enhancing innate immunity to bacterial infection in this population, or perhaps a therapeutic adjunct in patients diagnosed with tuberculosis.

Studies have also linked low serum vitamin D to rheumatoid arthritis, multiple sclerosis, diabetes, cardiovascular disease, and colon, prostate, and breast cancer, Dr. Modlin noted. There is considerable interest in investigating the potential of vitamin D supplementation in those diseases, and in atopic dermatitis as well.

'I would just say, "Vitamin D: It does an immune system good." '
DR. MODLIN

The antimicrobial peptide cathelicidin is normally present in human epidermis. Investigators at the University of California, San Diego, have shown that cathelicidin expression by macrophages, monocytes, and keratinocytes is low in atopic dermatitis patients, and that cathelicidin levels rise in response to oral vitamin D supplementation, he continued.

On the other hand, investigators at M.D. Anderson Cancer Center, Houston, have documented high cathelicidin levels in psoriasis patients; they suggest overproduction of cathelicidin leads to the highly inflammatory response characteristic of psoriasis. So it is possible that high vs. low expression of cathelicidin helps account for the strikingly different disease manifestations that define these two common inflammatory dermatologic diseases, Dr. Modlin said.

Numerous epidemiologic studies have documented the high prevalence of vitamin D insufficiency, both in the public at large and in populations with various diseases. Modern life is increasingly incompatible with vitamin D sufficiency.

More sun exposure is the most efficient route to higher vitamin D levels, Dr. Modlin said, but as a dermatologist, he isn't enthusiastic about that as a solution.

Dr. Modlin often is asked what constitutes appropriate supplementation. He noted that in a recent reasoned and comprehensive review of vitamin D deficiency, Dr. Gerry Schwalfenberg, a family physician at the University of Alberta, Edmonton, concluded that a healthy blood level of vitamin D is 80-100 nmol/L and that most normal individuals who don't spend a lot of time in the sun need at least 1,000 IU daily to achieve that (Can. Fam. Physician 2007;53:841-54).

Dr. Modlin believes those figures are too low.

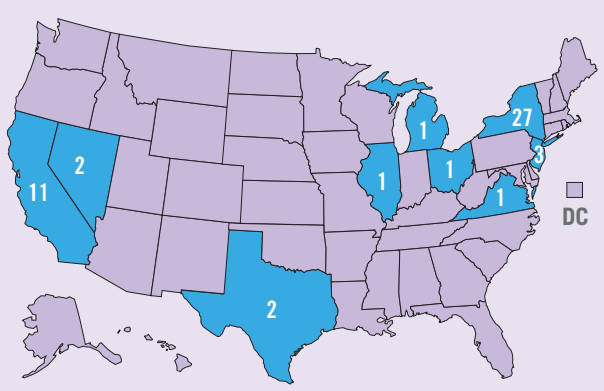
"I think we need to get above 100 nmol/L, and we probably need 2,000 IU daily to maintain that. That's equivalent to 40 glasses of milk," Dr. Modlin pointed out at the meeting of the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

"Most endocrinologists think our serum vitamin D levels are too low, but the U.S. government won't let us get to 100 nmol/L," he said.

"I know I'm not getting enough UV on the UCLA tennis courts with the sunscreen I'm wearing. And the [National] Dairy Council slogan, 'Milk: It Does a Body Good'—I'm not sure about that, either. I would just say, 'Vitamin D: It does an immune system good,' " he concluded. ■

DATA WATCH

Number of Reported Cases of Extensively Drug-Resistant Tuberculosis



Note: Based on 1993-2006 data.
Source: Centers for Disease Control and Prevention

ELSEVIER GLOBAL MEDICAL NEWS

FDA Approves Rapid Test to Detect Flu

BY LORINDA BULLOCK
Associate Editor

The Food and Drug Administration approved a new test that can diagnose human influenza infections, including the highly pathogenic influenza A (H5N1) virus, and produce results within 4 hours.

The device, known as the Human Influenza Virus Real-Time RT-PCR Detection and Characterization Panel (rRT-PCR Flu Panel), was developed by the Centers for Disease Control and Prevention. It is able to detect and identify the most commonly circulating human influenza viruses using a molecular biology technique that can "differentiate between seasonal and novel influenza," according to a written statement released jointly by the FDA and CDC.

The ability to distinguish those differences facilitates speedier diagnoses, Dr. Frank Torti, FDA principal deputy commissioner and chief scientist, said in the statement.

"It will also provide qualified laboratories with a means to rapidly detect new influenza viruses that have not been identified yet and that could pose a pandemic risk," Dr. Torti commented.

The new test will give laboratories 'a means to rapidly detect new influenza viruses that have not been identified yet and that could pose a pandemic risk.'

Dr. Julie Gerberding, director of the CDC, emphasized the value of having a tool that can test multiple samples at the same time and produce results faster.

Representatives of the FDA and the CDC said the device isolates and amplifies viral genetic material present in secretions taken from a patient's nose or throat. That material is analyzed by another device, called the Applied Biosystems 7500 Fast Dx, which was approved simultaneously with the rRT-PCR Flu Panel.

The test will be available to CDC-qualified laboratories as soon as the end of this year. Some labs will be eligible to receive reagents free of charge to aid in the testing process.

The CDC, Applied Biosystems Inc., and the Association of Public Health Laboratories collaborated on the development of the new test.

The H5N1 virus is of particular concern to researchers because it can circulate widely among people, raising the threat of a pandemic.

According to World Health Organization data, there have been 387 cases and 245 deaths from the virus worldwide since 2003. ■

Ample Supply of Tamiflu Available for 2008-2009 Season

A sufficient amount of the prescription antiviral medication oseltamivir will be available throughout the United States during the upcoming flu season, according to a statement released by its manufacturer, Roche.

Oseltamivir (Tamiflu) can be distributed to pharmacies with low supplies of the drug within 24 hours through a rapid response system that Roche has set up through distributors nationwide.

The drug is indicated for the treatment and prevention of influenza in adults and children aged at least 1 year.

It is the only oral antiviral medication with this indication that is recommended by the Centers for Disease Control and Prevention.

Oseltamivir must be administered within the first 48 hours of flu symptoms in order for it to be effective. It is designed to be active against all clinically relevant influenza virus strains by preventing the virus from spreading inside the body.

—Jeff Evans