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Vitamin D critical to human TB response

Findings illuminate possible prevention pathways

By Alvin Powell
Harvard News Office

Vitamin D plays a critical role in the human body's response to tuberculosis, according to new research that explains why people of African descent are more susceptible to TB.

The research also suggests a new way to fight one of the world's deadliest diseases: with a simple dietary supplement. Tuberculosis, usually caused when a person inhales tuberculosis bacteria, killed an estimated 1.7 million people in 2003 and is the leading cause of death for people afflicted with AIDS, according to the World Health Organization (WHO).

People of African descent are more susceptible to tuberculosis than Caucasians, with higher rates of infection and more severe cases once infected, trends that had puzzled researchers until now. Sub-Saharan Africa, for example, has the world's highest per capita rates of both tuberculosis cases and deaths from the disease, roughly twice the next-highest region, according to WHO statistics.

The research, conducted by a team from the University of California, Los Angeles (UCLA), and the Harvard School of Public Health, shows that vitamin D plays a key role in the production of a molecule called cathelicidin, which kills the tuberculosis bacteria.

The body produces vitamin D when sunlight hits the skin. The skin pigment melanin - more abundant in darker skin - shields the body from the sun's rays, reducing damage from ultraviolet light, but also reducing vitamin D production.

The mechanism by which the human body fights tuberculosis had eluded researchers for years. Harvard School of Public Health Dean Barry Bloom, an immunologist and a co-author of the Science Express paper detailing the research, led a team in 1992 that discovered that mouse immune cells produce nitric oxide to fight tuberculosis.

Since the laboratory mouse has proven a reliable model for many different human diseases and conditions, the finding sent researchers searching for a similar mechanism in humans, to no avail. The current findings explain why mice and humans have different mechanisms to fight TB - mice are nocturnal so they evolved a way that was not dependent on sunlight.

The research also showed why sanitariums - in sunny locations high in the mountains - were a traditional method of treating people with TB, Bloom said. With the advent of modern medicine in the 20th century, the idea of sitting people on a porch in the sun fell out of favor, but the current research suggests why the idea may have had some benefit.

Bloom said the breakthrough came with researchers from UCLA, who did a genetic screening of two types of human immune cells to see which genes are switched on when the cells come in contact with tuberculosis.

The results surprised researchers. Most studies of different cells' responses to the same stimulus show tens or hundreds of different genes switched on or off. But Bloom said this study showed just two.

Further examination showed that one of the differences was the activation of the gene encoding the vitamin D receptors that is expressed on the surface of an important immune cell called a macrophage. When the receptor was activated, it started a complex chain reaction within the cell that changed vitamin D from a passive to an active form. The newly activated vitamin D, in turn, sliced a pre-existing protein in two. One of the resulting chunks of that protein is the tubercle bacillus-killer cathelicidin.

The researchers went on to test the response of cells cultured in serum donated by African Americans and found that they produced 63 percent less cathelicidin than cells cultured in serum donated by whites. Adding a vitamin D precursor to the African-American serum increased cathelicidin production.

Bloom cautioned that the results are limited to the lab at this point, but said they were promising enough that clinical trials to test whether vitamin D supplements can help fight tuberculosis in people may be warranted.

Even with that caution, however, Bloom said it is exciting to discover that a dietary supplement costing just pennies - which can be rapidly distributed to areas of need - may be instrumental in reducing the frequency and severity of one of the world's deadliest diseases.

"It is unbelievably appealing: low-cost, low-tech, and easy to distribute," Bloom said.

http://www.news.harvard.edu/gazette/2006/03.09/01-tb.html