

## **New Roles of Vitamin D**

Vitamin D is a fat-soluble vitamin commonly associated with maintaining blood levels of calcium and the prevention of rickets. The “sunshine vitamin” is generally acquired by the body in two ways: sun exposure and dietary intake. Foods of animal origin are primary food sources, including liver, beef, veal, eggs, vitamin D-fortified foods and saltwater fish.<sup>1</sup> Food sources contain relatively low levels of vitamin D. Exposure to sunlight is our primary method of receiving vitamin D. People living in areas with less sunlight due to geographic location, cloud cover and other factors should consider vitamin D supplements. Those who receive enough sun exposure for adequate vitamin D production must not receive overexposure, which carries its own health risks.

New research suggests that vitamin D may play roles in the prevention of infections, cancer and multiple sclerosis (MS). Several epidemiological studies demonstrate a higher risk of several health ailments in populations with reduced exposure from the sun.

Vitamin D acts as an innate immune system modulator.<sup>5</sup> The innate immune system is the first line of defense against infection. Humans encounter potential disease-causing agents called pathogens regularly, but seldom do they cause disease. Most pathogens are destroyed by the innate immune system within minutes or hours after contact as it provides broad-spectrum (non-specific), short-lasting protection.<sup>6</sup>

The most important known role of vitamin D in innate immunity involves its ability to stimulate the expression of cathelicidin, an antimicrobial peptide produced in immune cells and the epithelial cells lining the respiratory tract.<sup>7,8</sup> Cathelicidin expression is generally associated with inflammation.<sup>9,10</sup> A study published in August 2006 demonstrated for the first time that vitamin D-induced cathelicidin expression produced innate antimicrobial activity independent of the release of pro-inflammatory molecules and did not result in inflammation.<sup>11</sup>

Vitamin D supplementation is most needed in the fall and winter months when we get the least sun exposure and when infections are most prevalent. Unfortunately, sufficient human studies examining the correlation of vitamin D status and infections have not been done. However, two papers published between 1949 and 1956 suggest that vitamin D may lessen the frequency and duration of the flu in animal models.<sup>12,13</sup> Recent attention to vitamin D should prompt further investigation.

Good epidemiological evidence supports the theory that living at latitudes closer to the equator decreases the risks of many cancers such as prostate, colon, breast, endometrial, skin and pancreatic.<sup>14</sup> Observations over the last 65 years have shown an increased association between sufficient sun exposure and cancer risks.<sup>15</sup> In 1941, researchers noticed that people living at latitudes farther from the equator had an overall greater risk of dying from cancer than men and women of similar ages living at lower latitudes. This observation began to gain more attention in the 1980s when it was reported that risks of colon and breast cancers increased in higher-latitude populations.<sup>16</sup>

One study examining the amounts of vitamin D-producing UV light in seven different areas of the U.S. showed a clear difference during the winter months (November through February) based on latitude. At higher latitude locations (>25 degrees N), vitamin D-producing UV decreased dramatically compared to the eight warmer months. The lower latitude locations (<25 degrees N) showed no difference between the winter and warm months.<sup>17</sup> A prospective study revealed that in populations with less vitamin D being formed from UV exposure, low levels of vitamin D in the blood increase the risk of cancer two-fold. Men and women with higher blood levels of vitamin D are also less likely to die prematurely as a result of cancer.<sup>16</sup>

We do not completely understand how vitamin D works as an anti-carcinogenic. Several mechanisms are known, such as promoting programmed cell death in abnormal cells (apoptosis), promoting cell differentiation, inhibition of cell proliferation in malignant cell lines, inhibition of blood vessel growth, stimulating the mutual adherence of cells, and enhancing cellular communication through gap junctions.<sup>2,18</sup> (Gap junctions are intercellular channels that allow for the transfer of ions and other small molecules from cell to cell.) In the initial stages of carcinogenesis, mutagenic changes may occur that result proliferation of cells unable to communicate through gap junctions. Lack of mutual cell adherence and communication through gap junctions inhibits apoptotic, growth-suppressing and cell-differentiating signals from neighboring cells.<sup>19</sup> A recently published study of malignant breast epithelial cells in culture demonstrated vitamin D's promotion of apoptosis and differentiation, as well as inhibition of proliferation.<sup>20</sup> The effectiveness of vitamin D has been found to be dose-dependant.<sup>2</sup>

Multiple sclerosis (MS) is an autoimmune disease involving inflammation that leads to the destruction of the myelin sheaths that surround and protect nerve fibers of the central nervous system (CNS).<sup>19</sup> This disease occurs most frequently in geographic areas farthest from the equator, which suggests that vitamin D may protect against it.<sup>20-22</sup> Very few treatments or particular diets have been shown to effectively counter MS. However, certain deficiencies in nutrients like vitamin D may potentially worsen MS symptoms.<sup>23</sup>

Very little information is available regarding the role of vitamin D in brain development. The white matter and branching cells called oligodendrocytes in the brain have been shown to be responsive to vitamin D and contain vitamin D receptors. It has been suggested that low levels of vitamin D during the development of oligodendrocytes may cause unnecessary death of these cells.<sup>20</sup> Death of oligodendrocytes is devastating to the CNS, since these cells are known to form myelin.

Although the relationship between the increased frequencies of MS in populations most susceptible to vitamin D deficiencies has been observed for more than 25 years, it has not yet been thoroughly examined. A number of epidemiological studies have confirmed that both exposure to sunlight during early life and vitamin D supplementation reduce the prevalence of MS in women.<sup>20</sup> Another study involving rats with experimental autoimmune encephalomyelitis (EAE), which is the animal model of MS, used a vitamin D treatment that reduced and even prevented the disease.<sup>21,22</sup> In a recent study,

researchers looked at 12 years of blood samples from US Army and Navy personnel and examined vitamin D levels and reported cases of MS in the Army physical disability database. The results showed clearly a reduced risk of MS in Caucasians with increasing blood levels of vitamin D. <sup>24</sup>

More well-designed clinical trials are needed in order to determine if vitamin D deficiency increases risks of infections and if vitamin D supplements can be cancer- and MS-preventive. Supplemental vitamin D may offer a cost-effective and practical way to reduce the occurrence and symptoms of several diseases in the future. Other new areas of vitamin D research include type I diabetes, inflammatory bowel disease, rheumatoid arthritis, lupus and cardiovascular disease.

## **References**

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