MENTAL HEALTH

Vitamin D receptors and vitamin D metabolizing enzymes are present in the central nervous system. Calcitriol (the active vitamin D hormone) affects numerous neurotransmitters and neurotrophic factors, relevant for mental disorders. In the case of depressive disorders, considerable evidence supports a role of suboptimal vitamin D levels. However, the data are not conclusive and further studies are necessary. Especially, the relative importance of the pineal-melatonin system versus the vitamin D-endocrine system for the pathogenesis of seasonal affective disorders is presently unresolved. Two diagnoses, schizophrenia and autism, have been hypothetically linked to developmental (prenatal) vitamin D deficiency, however, also in adult patients, low levels have been reported, supporting the notion that vitamin D deficiency may not only be a predisposing developmental factor but also relate to the adult patients' psychiatric state. Two cases are described, whose psychiatric improvement coincided with effective treatment of vitamin D deficiency.

CARDIAC DISEASE

Pilz et al reported that severe vitamin D deficiency was strongly associated with sudden cardiac death, cardiovascular events and mortality, and that there were borderline associations with stroke and fatal infection. In agreeing with this, Kulie stated that "low vitamin D levels are associated with increased overall and cardiovascular mortality."

Cardiovascular problems, particularly hypertension and coronary heart disease, occur at higher rates with increased distance from the equator. Prevalence of vitamin D deficiency also increases the farther away one lives from the equator. Vitamin D affects many tissues and systems critical to cardiovascular health, suggesting its critical role in heart health.

For several decades it has been noted that there are higher rates of hypertension and coronary heart disease with increasing distance from the equator. This phenomenon has been attributed to the higher prevalence of vitamin D deficiency in regions with less sunlight exposure. Several lines of biological evidence link vitamin D deficiency with abnormalities of cardiovascular structure and function. Vitamin D has actions on numerous tissues in the body, including the endothelium (the cells that line the vessel walls) and cardiomyocytes (heart muscle cells). Vitamin D appears to regulate the tendency for these cells to divide and proliferate. Genetically engineered mice that are deficient in vitamin D develop hypertension and abnormal heart structure. Vitamin D also has an important influence on several signaling pathways in the body that interact with the cardiovascular system. Experimental vitamin D deficiency leads to upregulation of inflammatory cells, which ultimately promote the development of atherosclerosis and other vascular abnormalities. Furthermore, vitamin D is an important inhibitor of the renin-angiotensin system. Activation of the renin-angiotensin system, observed in experimental models of vitamin D deficiency, leads to increased blood pressure and thickening of the heart chambers.
VITAMIN D

TUBERCULOSIS & INFECTIOUS DISEASE

A role for vitamin D in host defense in human TB is suggested by correlation of serum 25(OH)D levels with disease outcome, VDR polymorphism studies and therapeutic intervention studies with vitamin D. In a study of Indonesian patients with active TB, the patients with the highest 25(OH)D levels at the outset of therapy had “less active pulmonary disease.”

Two major VDR polymorphisms have been studied in terms of TB susceptibility, TaqI and FokI, with conflicting results. However, investigation of the relationship between vitamin D deficiency and VDR polymorphisms with tuberculosis in the Gujarati Asians living in west London revealed that certain VDR genotypes, both the TaqI tt and FokI ff alleles, correlated with disease only when 25(OH)D levels were deficient. Successful vitamin D therapy for mycobacterial infections includes the treatment of patients with lupus vulgaris (a form of cutaneous TB) with oral vitamin D2, as well as the combination of vitamin D with standard chemotherapy in pulmonary TB.

More studies are required to determine whether vitamin D supplementation is of potential use in the prevention and/or treatment of tuberculosis, as well as other infectious diseases such as influenza in which serum vitamin D levels may influence susceptibility.

AUTOIMMUNE DISEASES

Pierrot-Deseilligny claimed that “it can no longer be ignored that many multiple sclerosis (MS) patients have a lack of vitamin D, which could be detected and corrected using an appropriate vitamin D supplementation. Vitamin D supplementation appears to improve the general state of these patients. It has been suggested that a reduction in the number of cases of MS could be reduced through vitamin D supplements.”

Autoimmune diseases also are more prevalent farther from the equator. Vitamin D has been shown to influence dendritic cell function; it is these cells that either direct the immune system to tolerate or attack a particular cell or protein, which may explain the link between vitamin D deficiency and autoimmune diseases.

Vitamin D has a strong influence on D-cell function. D-cells direct the immune response to behave with tolerance to a given cell or protein, when vitamin D concentrations are normal. If there is not enough vitamin D around these cells, that could lead the rest of the immune system in a defensive or inflammatory response to a given cell or protein. If the immune system during the late stages of pregnancy or in the first year of life does not have enough vitamin D around, it may not recognize or develop tolerance to a variety of normal proteins and cells in the body, including some of the bacteria in the gut, skin and airways.

Research shows that the further away from the equator a person spends the first 15 years of life, the higher the risk for developing MS. This suggests that sunlight and vitamin D early in life are important for normal immune system development. A study from Harvard University on military recruits showed a 64% lower risk of developing MS with vitamin D levels above 40 ng/mL, and in recruits under 20 years of age the risk reduction was more than 90%.
Vitamin D has long been considered a critical nutrient for pregnant women due to its importance in proper skeletal formation, but it is now known to play an even more important role in nurturing a healthy fetus.

The current recommended amount is 200 IU/d, but if a pregnant woman receives only that amount, she and the fetus will both be deficient compared to the desired 32 ng/ML circulating 25(OH)D level. The correct amount is probably closer to 2,000-4,000 IU/d for a pregnant woman, and even more for a lactating woman (precise amounts vary based on skin color, sunlight exposure, sunscreen use, latitude, etc.). In fact, three recent studies in which Dr. Hollis was involved—currently being prepared for publication but presented at the May Pediatric Academic Society meeting in Vancouver—showed that pregnant women who were supplemented with higher levels of vitamin D had less incidence of bacterial infections, less pre-term labor, and less complications of pregnancy (pre-eclampsia, diabetes and hypertension).

“The best outcomes were from the group that took 4,000 IU/d, and we saw not a single adverse event due to vitamin D intake,” Dr. Hollis explains.

If a pregnant woman only receives a prenatal vitamin containing 400 IU of vitamin D, both she and her fetus will be vitamin D deficient by today’s definition of 32 ng/ml circulating 25(OH)D. How much vitamin D is required to replete and maintain the pregnant women is probably between 2,000-4,000 IU/D and will be dictated by skin color, season, latitude, outdoor activity, weight and sunscreen usage. One factor that will not influence it is diet, as vitamin D is largely absent in the foods that humans normally eat. A pregnant woman with a circulating 25(OH)D level <32 ng/ml increases the fetus’ risk for many long-latency diseases such as multiple sclerosis, type I diabetes and impaired neurodevelopment including autism. Vitamin D deficiency during pregnancy may also put the mother at risk of developing intrauterine infections.

An arbitrary AI has been set at 200 IU/d during lactation. Students of nutrition are taught that human milk is the perfect food for the human newborn; however, it is deficient in vitamin D because the mothers making the milk are deficient. This occurs when mothers only obtain a vitamin D intake of 200-400 IU/d. When milk from these deficient mothers is the only source of vitamin D to the nursing infant, the nursing infant develops profound vitamin D deficiency. How much vitamin D should a lactating mother obtain to ensure adequate amounts of vitamin D for herself and her nursing infant? Current research points to an intake of at least 6,000 IU/d of vitamin D3.
Basic science studies have provided understanding, albeit not all of the details, of a mechanism for a vitamin D anticancer effect. Most of our vitamin D is made in the skin upon exposure to sunlight. In addition, a small amount is ingested in food. Vitamin D from both sources is converted by the liver to 25(OH)D. Many cells in the body are able to convert 25(OH)D into its active form, 1,25(OH)2D. Most of these same cells possess vitamin D receptors (VDRs). The freshly synthesized 1,25(OH)2D binds to the VDR and ultimately leads to production of a myriad of proteins. Some of these proteins are responsible for cell proliferation, differentiation and programmed cell death, activities necessary for initiation and promotion of cancer. Adequate serum 25(OH)D is likely to be necessary for the proposed anticancer effect of vitamin D.

Lower concentrations of vitamin D have been found to be linearly associated with higher risk of death in patients with breast cancer and significantly higher risk of distant recurrence.

Vitamin D intake also was associated with a lower risk of pancreatic cancer, but studies of plasma or predicted vitamin D level or dietary intake have generally not been supportive of a major role of vitamin D status in middle-age or elderly men on prostate cancer risk. A study of men with prostate cancer found that men in the lowest vitamin D quartile were more likely to die of their cancer compared to those in the highest quartile.

Vitamin D deficiency can increase the risk of bone fractures, rickets, and osteoporosis.

It causes rickets in children (even in the U.S.) and will precipitate and exacerbate osteopenia, osteoporosis and fractures in adults. A sufficient amount of vitamin D, therefore, prevents rickets in children and osteomalacia in adults. With supplemental calcium, it also helps protect older adults from osteoporosis. Insufficient intake can result in thin, brittle or misshapen bones. Craney et al presented a meta-analysis of some 100 articles on the value of vitamin D supplements and found “fair evidence from studies of an association between circulating vitamin D concentrations with some bone health outcomes [established rickets, falls and bone mass density (BMD)].”