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Vitamin D Status and the Metabolic Syndrome

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ABSTRACT

The identification of vitamin D receptor expression in different tissues suggests a widespread role for vitamin D action beyond its classical function in bone and mineral metabolism. Recently, the importance of vitamin D status as a risk factor in the development of metabolic syndrome has been the focus of several studies.

Key words: hypertension, insulin resistance, obesity, vitamin D deficiency

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VITAMIN D SYNTHESIS AND METABOLISM

During exposure to sunlight, ultraviolet B (UVB) photons penetrate into the skin and are absorbed by 7-dehydrocholesterol, inducing the formation of pre-vitamin D (Figure 1). This is an unstable form of vitamin D that rapidly undergoes rearrangement to form vitamin D_3 (cholecalciferol). Vitamin D_2 (ergocalciferol) is the form of vitamin D that occurs in plants and is used to fortify certain foods such as fluid milk. Both vitamin D forms eventually enter the circulation bound to a vitamin D-binding protein and are metabolized in the liver by the vitamin D-25-hydroxylase enzyme (25-OHase or CYP27A1) to 25-hydroxyvitamin D (calcidiol), the main vitamin D form circulating in plasma and a substrate for production of the hormonally active metabolite 1,25-dihydroxyvitamin D (calcitriol).

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The metabolic conversion in the body of the pro-hormone 25-hydroxyvitamin D to the active hormonal form, 1,25-dihydroxyvitamin D, is accomplished by the P_{450} family enzyme 25-hydroxyvitamin D-1α-hydroxylase (CYP27B1), which is found mainly in the kidney but is also present to some extent in other cell types, such as immune cells, colon cells, placenta, breast, prostate, and pancreas. Plasma pro-hormone 25-hydroxyvitamin D concentrations are 1000 times greater than that of the steroid hormone calcitriol and have a much longer biological half-life: around 2 to 3 weeks compared with 4 to 6 hours for the hormone. Because of this relative stability, the principal biomarker used to assess vitamin D status is plasma 25-hydroxyvitamin D concentration. Moreover, because the activity of renal 1α-hydroxylase is tightly controlled to regulate plasma calcium homeostasis, the potential for a local autocrine or paracrine action from the non-renal cellular production of 1,25-dihydroxyvitamin has engendered much enthusiasm as a possible explanation for the reduction in chronic disease risk associated with greater solar radiation exposure or higher vitamin D status found in some studies.

It is well recognized that latitude, season, and time of day exert a major influence on cutaneous vitamin D_3 production. During summer months, 7-dehydrocholesterol in the skin is most efficiently converted to pre-vitamin D_3.[1] Latitude relative to the equator is often assumed to be one the most important factors influencing vitamin D status. Photosynthesis of vitamin D in the skin is higher in low-latitude regions due to more UVB radiation exposure. However, living in a sunny climate alone does not eliminate low serum vitamin D levels.[2] Other factors such as use of sunscreen, the amount of melanin in the skin, the type of clothing worn, and any other situation that reduces cutaneous UVB radiation exposure will reduce the cutaneous production of vitamin D_3.[3,4] During the summer, sunlight is capable of producing vitamin D_3 from 0700 to 1700 h, with a peak rate of synthesis of pre-vitamin D at 1230 h.[5] There is a significant variation in the prevalence of inadequate vitamin D status during summer and winter and at different latitudes and dietary vitamin D intakes.[6]

Unfortunately, natural dietary sources of vitamin D (Table 1) are limited, thereby increasing the risk of

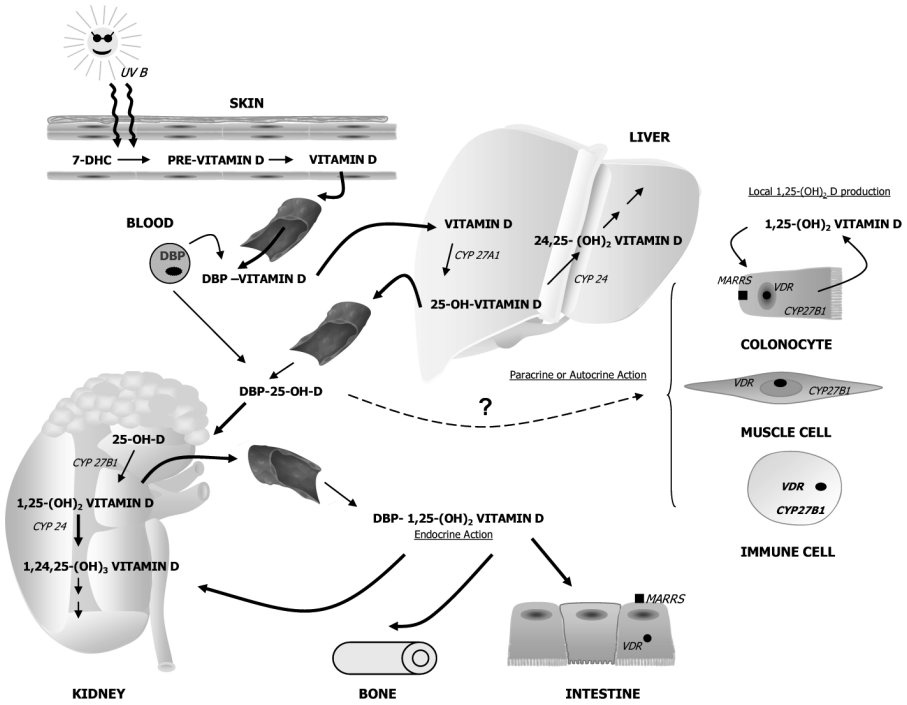

Figure 1. Cutaneous synthesis and metabolism of vitamin D. In the skin, 7-dehydrocholesterol (DHC) can be converted to pre-vitamin D in response to ultraviolet B (UVB) radiation from the sun. Pre-vitamin D is then converted to vitamin D. Continued cutaneous exposure to UVB can produce various photoproducts (not shown) from both pre-vitamin D and vitamin D. Vitamin D (and other vitamin D metabolites) are carried in the blood by a 50-kD vitamin D-binding protein. Vitamin D is converted in the liver by the P_{450} enzyme CYP27A1 to 25-hydroxyvitamin D (25-OH-vitamin D), which is the major form of vitamin D found in the blood. In the kidney, another P_{450} enzyme, CYP27B1, adds a hydroxyl group at the C-1 position of 25-OH-vitamin D to form the active vitamin D hormone 1,25-dihydroxyvitamin D, or 1,25-$(OH)_2$ vitamin D. Both 25-OH-vitamin D and 1,25-$(OH)_2$ vitamin D are hydroxylated at C-24 by CYP24, which initiates their inactivation and metabolic breakdown. Vitamin D receptor (VDR)-mediated gene expression in response to 1,25-$(OH)_2$ vitamin D occurs in many different tissues, including classical vitamin D target organs such as intestine, bone, and kidney. The active vitamin D hormone can also stimulate very rapid changes at the plasma membrane that are mediated by a 1,25-$(OH)_2$ vitamin D membrane-associated rapid response steroid hormone binding protein (MARRS). Finally, there is also evidence to show that CYP27B1 is found in some non-renal cell types and therefore may afford an opportunity for local 1,25-$(OH)_2$ vitamin D to be formed from 25-OH-vitamin D, suggesting the possibility of a vitamin D paracrine or autocrine pathway.

developing vitamin D deficiency in the absence of adequate cutaneous vitamin D production or the consumption of vitamin D-fortified products. Some foods fortified with vitamin D in the United States include milk and some orange juices, cereals, breads, yogurts, and cheese products. The recommended Adequate Intake (AI) of vitamin D for children and adults is 200 IU/d (5 μg/d), whereas for adults 51 to 70 years of age it is 400 IU (10 μg/d), and for adults up to 71 years of age it is 600 IU (15 μg/d). Data from NHANES III and the Continuing Survey of Food Intakes by Individuals (CSFII)[7] indicate adequate intakes in children, adolescents, and adults until age 50. However, the mean vitamin D intake in elderly men and women are under recommended values even when the use of supplements is considered (men 51–70 years of age = 8.0 ± 0.27 μ/d and ≥ 71 = 8.3 ± 0.27 μ/d; women 51–70 years of age = 7.8 ± 0.24 μ/d and ≥ 71 = 8.1 ± 0.57 μ/d).

Table 1. Food Sources of Vitamin D

Food	Serving	Vitamin D *IU*
Cod liver oil	1 TBS	1360
Salmon, canned, pink	3 oz	360
Sardines, canned	3 oz	250
Mackerel, canned	3 oz	214
Tuna, canned	3 oz	200
Milk, fortified	1 cup	100
Orange juice, fortified	1 cup	100
Margarine, fortified	2 tsp	50
Cereal, fortified	1 cup	40
Liver, beef, cooked	3.5 oz	30
Egg	1 whole	20

DEFINING OPTIMAL VITAMIN D STATUS

Establishing biochemical criteria for vitamin D deficiency or insufficiency is still a matter of debate. The

establishment of so-called normal serum "vitamin D" values based on the population distribution of serum 25-hydroxyvitamin D is not appropriate, because serum 25-hydroxyvitamin D reflects the degree of sun exposure, geographic location, and level of dietary vitamin D intake of the population. However, it is known that inadequate vitamin D status can result in poor calcium absorption, relative hypocalcemia, and compensatory increases in serum parathyroid hormone (PTH). One apparent area of consensus in the vitamin D field has been that circulating 25-hydroxyvitamin D should exert maximal suppression of circulating PTH, with greatest calcium absorption, in order to promote adequate bone metabolism.[8] However, the definition of vitamin D insufficiency and desirable serum 25-hydroxyvitamin D levels can differ among investigators (Table 2), creating some confusion in the estimate of the population prevalence of suboptimal vitamin D status. Desirable levels of circulating 25-hydroxyvitamin D have been variously defined as 50, 80, and higher than 100 nmol/L.[8] Vitamin D "insufficiency" can range from less than 40 to 80 nmol/L. Vitamin D "deficiency" has generally been defined as a serum 25-hydroxyvitamin D concentration under 25 nmol/L (10 ng/mL). Moreover, this latter cutoff value can be supported by the observation that serum 1,25-dihydroxyvitamin D, the active hormonal form of vitamin D, is positively correlated with serum 25-hydroxyvitamin D up to about 30 nmol/L,[9] suggesting a limitation of adequate hormonal substrate at these low 25-hydroxyvitamin D concentrations.

The prevalence of insufficient or deficient vitamin D status is alarmingly high in some groups. Analysis of the prevalence of vitamin D insufficiency (defined in this case as serum 25-hydroxyvitamin D under 37.5 nmol/L [15 ng/mL]) among healthy, ambulatory, nonpregnant women between the ages of 15 and 49 years who participated in the NHANES III survey was only 4.2% in white women, but was 42.4% in black women. The prevalence of vitamin D deficiency (defined in this case as a serum 25-hydroxyvitamin D under 20 nmol/L [8 ng/mL]) was only 0.5% in white women, but was 12.2% in black women.[10] However, the prevalence of vitamin D deficiency can be much higher in other vulnerable groups. For example, in sun-deprived, homebound elderly people either living in nursing homes or community dwelling, the prevalence of vitamin D deficiency (serum 25-hydroxyvitamin D $\leq$ 25 nmol/L [10 ng/mL]) was between 38% and 54%.[11]

Table 2. Classification of Vitamin D Status According to Serum 25-Hydroxyvitamin D Concentration (nmol/L)*

Sufficient	Insufficient	Deficient	Reference
>100	<50	<25	McKenna, 1998[52]
>40	<40	<25	Vieth, 1999[53]
>50	<50	<25	Lips, 2001[2]
>80	<80	—	Heaney, 2003[54]

* Values are adapted from references.

The importance of race, irrespective of body weight, on serum 25-hydroxyvitamin D has been recently highlighted using data from 6402 adolescent and adult females from the Third National Health and Nutrition Examination Survey (NHANES III, 1988-1994).[12] After adjusting for total body fat percentage (%TBF), serum 25-hydroxyvitamin D was 1.3 to 1.9 times higher in white women compared with black women. Interestingly, in this study, a regression analysis of serum 25-hydroxyvitamin D on %TBF separated by race and adjusted for age and other confounders found that %TBF was significantly related to serum 25-hydroxyvitamin D in white women, but in black women the relationship was significant only among women less than 50 years old. These findings suggest that the relationship between body fat and serum 25-hydroxyvitamin D may be complex.

VITAMIN D STATUS AND METABOLIC SYNDROME

Low vitamin D status is being increasingly recognized as widespread in all life stages, even in sunny climates.[2,4] The possible importance of vitamin D status as a novel risk factor for various chronic diseases has gained more interest. One area of recent study has been the investigation of the association between vitamin D status and the metabolic syndrome. The National Cholesterol Education Program's Adult Treatment Panel III Report (NCEP/ATP III) defines the metabolic syndrome as a multiplex of risk factors for cardiovascular disease comprised of six major components[13]:

- Abdominal obesity
- Atherogenic dyslipidemia
- Raised blood pressure
- Insulin resistance with or without glucose intolerance
- Proinflammatory state
- Prothrombotic state

The presence of at least three of the following five specific criteria indicates the presence of metabolic syndrome in an individual: 1) waist circumference $>$ 102 cm in men and $>$ 88 cm in women; 2) hypertriglyceridemia $\geq$ 150 mg/dL (1.695 mmol/L); 3) HDL cholesterol $<$ 40 mg/dL (1.036 mmol/L) in men and $<$ 50 mg/dL (1.295 mmol/L) in women; 4) blood pressure $\geq$ 130/85 mmHg; and 5) high fasting serum glucose $\geq$ 110 mg/dL ($\geq$ 6.1 mmol/L). In the case of fasting glucose levels, some investigators have used a cutoff value of $\geq$ 100 mg/dL (5.6 mmol/L).[13,14]

The prevalence of metabolic syndrome in the United States was 23.1% in NHANES III and 26.7% in NHANES 1999–2000.[14] It should also be noted that metabolic syndrome is not restricted to the elderly population. More than 2 million US adolescents currently have a metabolic syndrome phenotype.[15] The clinical significance of the metabolic syndrome remains controversial, however, because it is not clear if the syndrome is a disease or a constellation of risk factors.[14] The metabolic syndrome is viewed by some investigators as a metabolic complication of obesity, while others hold that insulin resistance is the major underlying risk factor.[13] In any case, this condition has important public health implications because of the well-known health risks associated with it. The evidence that the metabolic syndrome is an emerging condition among a large portion of the population makes the identification of risk factors an important priority. Recent epidemiologic findings suggest that low serum 25-hydroxyvitamin D, a measure of vitamin D status, is associated with an increased risk of metabolic syndrome.[16,17,18]

Based on a multistage, stratified sampling design, a representative sample of the US population participated in NHANES III (Third National Health and Nutrition Examination Survey). Ford et al.[16] recently reported the association in NHANES III between vitamin D status and the metabolic syndrome in 8421 men and nonpregnant women who were 20 years of age or older. To investigate the association between vitamin D status and the metabolic syndrome, the population was broken down on the basis of quintiles of serum 25-hydroxyvitamin D to ascertain whether the portion of the population with the metabolic syndrome differed by vitamin D status and to test for a linear trend. The association between metabolic syndrome and its components and serum 25-hydroxyvitamin D was examined by multiple logistic regression analysis to control for other potentially confounding factors. As expected, around 1 in 5 adult subjects had metabolic syndrome. The mean serum 25-hydroxyvitamin D concentration in those with metabolic syndrome was 67.1 nmol/L, which was significantly lower than that in subjects without metabolic syndrome, who had a mean serum 25-hydroxyvitamin D concentration of 75.9 nmol/L. After various statistical adjustments, the odds ratio of having the metabolic syndrome decreased progressively across increasing quintiles of 25-hydroxyvitamin D concentration (Figure 2). The study also found a significant inverse association for quintiles of serum 25-hydroxyvitamin D with some of the individual components of the metabolic syndrome, including abdominal adiposity, hypertriglyceridemia, and hyperglycemia.

In another recently published study, Liu et al.[18] analyzed data from 10,066 women 45 years of age or older who participated in the Women's Health Study to evaluate dietary vitamin D and calcium intake and its association with the prevalence of metabolic syndrome. Data were analyzed by quintiles of total calcium and vitamin D intake, and a logistic regression model was applied to examine the association between calcium and vitamin D intake and the risk of metabolic syndrome. The median calcium intake in this cohort was 857 mg/d and the median vitamin D intake was 266 IU/d (6.65 μg/d). The prevalence of metabolic syndrome components was lower in women in the highest quintile of combined calcium and vitamin D intake than in those in the lowest quintile. However, since there is a high correlation between dietary calcium and vitamin D intake, attempts were made to find the association between each of these nutrients and the risk of metabolic syndrome. Interestingly, an inverse association between dietary calcium and metabolic syndrome was observed in these women within each tertile of dietary vitamin D intake without significant interaction, suggesting that calcium intake (by means of dairy product consumption) was associated with a lower prevalence of the metabolic syndrome than vitamin D alone. However, the authors pointed out that the null findings for vitamin D intake may be attributed to an inadequate reflection of vitamin D intake on overall vitamin D status due to the lack of information on sun exposure. To what extent vitamin D status, irrespective of obesity, is involved in the pathogenesis of the metabolic syndrome and type 2 diabetes remains to be determined.

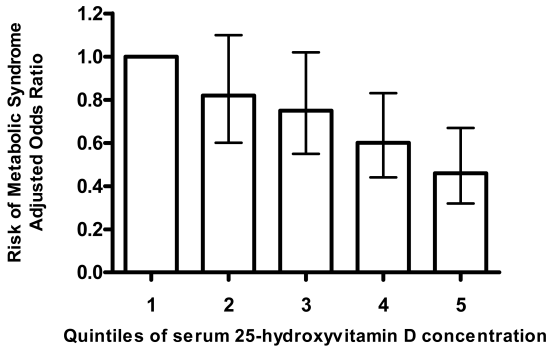

Figure 2. Association of vitamin D status with the risk of metabolic syndrome in the United States. Adjusted odds ratio and 95% confidence interval for the risk of having the metabolic syndrome based on data from NHANES III, 1988–1994 16 from 8421 US adults 20 years of age or older. Quintiles of serum 25-hydroxyvitamin D were: Quintile 1: $\leq$ 48.4 nmol/L; quintile 2: 48.5–63.4 nmol/L; quintile 3: 63.5–78.1 nmol/L; quintile 4: 78.2–96.3; and quintile 5: $\geq$ 96.4 nmol/L. Adjustments in the model were for age, sex, race or ethnicity, education, cotinine concentration, total cholesterol, C-reactive protein, alcohol use, physical activity, intake of fruits and vegetables, vitamin or supplement use, and season.

VITAMIN D INTERACTIONS WITH SOME COMPONENTS OF THE METABOLIC SYNDROME

Obesity

Adiposity is an important determinant of serum 25-hydroxyvitamin D and may be primarily responsible for the association between low vitamin D status and various disease outcomes, including the metabolic syndrome. Observations in both morbidly obese individuals and healthy people support a general association between adiposity and vitamin D status. The association between increased body fat and low serum 25-hydroxyvitamin D concentrations was recognized in humans and animal models more than 30 years ago,[19] and it was hypothesized that because vitamin D is a fat-soluble vitamin, it is sequestered and stored in fat tissues and muscle and then released slowly into the circulation. Twenty years ago, Bell et al.[20] demonstrated that the vitamin D-endocrine system in obese subjects is characterized by changes consistent with secondary hyperparathyroidism and increased serum 1,25-dihydroxyvitamin D. PTH is a peptide hormone secreted by the parathyroid gland in response to lower serum calcium concentrations, monitored by the extracellular calcium-sensing receptor in the parathyroid gland. PTH stimulates the renal 25-hydroxyvitamin D 1α-hydroxylase enzyme (CYP27B1) that carries out the C-1 hydroxylation of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D (the active steroidal hormone form of vitamin D) to stimulate the calciotropic effects of vitamin D and increase calcium absorption from the gut, renal calcium reabsorption, and calcium release from bone (Figure 1) to maintain serum calcium homeostasis. Bell et al.[20] hypothesized that increased levels of the active vitamin D metabolite was responsible for reducing serum 25-hydroxyvitamin D in obese individuals through a negative feedback inhibition of hepatic 25-hydroxyvitamin D synthesis. However, other potentially important determinants of serum 25-hydroxyvitamin D concentrations in obese people may be less sun exposure associated with limited mobility or clothing habits.[12,21]

Some years ago, Buffington et al.[22] evaluated vitamin D status in morbidly obese females and found low levels of serum 25-hydroxyvitamin D in 62% of the patients. Higher levels of PTH have also been observed in morbidly obese patients and were positively correlated with body mass index.[23] However, it is not only in the morbidly obese that there is an association between body fat and vitamin D status. Low serum 25-hydroxyvitamin D and elevated serum PTH in obesity was investigated recently in a population-based study by Snidjer et al.[21] Serum 25-hydroxyvitamin D, PTH, BMI, body composition (circumferences, skin-fold, and dual-energy x-ray absorptiometry [DEXA]) were evaluated in 237 men and 217 women. Total body fat was observed to be inversely associated with serum 25-hydroxyvitamin D and positively associated with serum PTH in both sexes. This association was even stronger when percentage of body fat derived from DEXA measurements was used. An association between body weight and serum 25-hydroxyvitamin D was also observed in 410 healthy women enrolled in a body composition study.[24] The mean body mass index of the study participants was 23.9 ± 2.9 kg/m^2, the mean TBF was 23.6 ± 7.3 kg, and the %TBF was $36.2\% \pm 7.4\%$. Serum 25-hydroxyvitamin D progressively decreased as the %TBF increased. After adjusting for age, race, season, and dietary vitamin D intake, a significant (albeit modest) negative correlation ($r = -0.13$) between serum 25-hydroxyvitamin D and %TBF was still present. Further investigation of this relationship in a stepwise linear regression analysis indicated that race played the primary role in predicting serum 25-hydroxyvitamin D, followed by season and then %TBF. These findings concerning the importance of race are consistent with the well-known observation that black persons have reduced synthesis of vitamin D in the skin due to the presence of more melanin, which absorbs some of the UVB radiation needed for cutaneous vitamin D synthesis.[25]

Glucose and Insulin Metabolism

Animal studies support a role for vitamin D in glucose and insulin metabolism. The vitamin D receptor is present in the pancreas.[26] Vitamin D deficiency impairs glucose- and arginine-induced insulin secretion in perfused rat pancreas.[27,28] In vivo, vitamin D-deficient rats have reduced glucose clearance and reduced insulin secretion in response to a glucose tolerance test.[29] Findings concerning the effects of vitamin D supplementation also support a relationship between vitamin D and insulin metabolism, including positive effects of vitamin D on blood glucose in diabetic animals.[30] Moreover, animal studies have provided evidence for a possible mechanism related to vitamin D and insulin metabolism,[31,32] suggesting that vitamin D deficiency reduces insulin turnover. Adequate vitamin D status facilitates the biosynthetic capacity of the β-cell and accelerates the conversion of pro-insulin to insulin. However, additional details of a possible molecular mechanism connecting vitamin D status and diabetes risk remain to be investigated.

Several investigations have found that people with impaired glucose tolerance[33,34] or diabetes[35] have lower concentrations of serum 25-hydroxyvitamin D than do subjects with normal glucose tolerance. The risk of type

2 diabetes increases in white and Mexican adults, but not in black adults, in the United States as vitamin D status declines.[36] A recent study in 753 postmenopausal women attending a university hospital outpatient clinic in Australia found an inverse association between fasting plasma glucose and serum 25-hydroxyvitamin D while controlling for age and BMI.[37] Chiu et al.[38] evaluated the association between serum 25-hydroxyvitamin D concentration and insulin sensitivity and β-cell function assessed by the 3-hour hyperglycemic clamp technique in 126 healthy, glucose-tolerant subjects, and found a positive correlation between 25-hydroxyvitamin D and insulin sensitivity index. They also observed that subjects with hypovitaminosis D (defined as plasma 25-hydroxyvitamin D levels lower than 20 ng/mL) had a significantly higher risk for components of the metabolic syndrome than did subjects without hypovitaminosis D. Extrapolating from their data, the authors suggested that an increase in plasma 25-hydroxyvitamin D from 10 to 30 ng/mL could improve insulin sensitivity by 60%. Vitamin D supplementation improved first-phase insulin secretion in type 2 diabetic patients.[39] Circumstantial support for an association between vitamin D and insulin function in humans is provided by the observation that the vitamin D receptor *Fok I* polymorphism in the translation initiation codon is associated with insulin sensitivity.[40]

Hypertension

Vitamin D may regulate blood pressure by regulating the renin-angiotensin system.[41] Vitamin D receptor knockout mice have elevated blood pressure and plasma renin activity.[42] In humans, there is a negative relationship between serum 1,25-dihydroxyvitamin D levels and plasma renin activity.[43] The INTERSALT study found a linear correlation between the rise in blood pressure or the prevalence of hypertension and latitude north or south of the equator, indicating a possible relationship between UV irradiation, cutaneous vitamin D synthesis, and blood pressure.[44] To better elucidate the vitamin D effect in hypertension, Krause et al.[45] exposed a group of hypertensive adults to a tanning bed that emitted UVA and UVB radiation similar to summer sunlight 3 times a week during 3 months. A control group was submitted to a tanning bed that only emitted UVA light similar to winter sunlight and no UVB radiation. They observed a significant increase in circulating 25-hydroxyvitamin D levels and a decrease in systolic and diastolic blood pressure in the group submitted to the UVA/UVB tanning bed treatment.

An 8-week vitamin D supplementation study in elderly women with low serum 25-hydroxyvitamin D found a 72% increase in serum 25-hydroxyvitamin D and a decreased systolic blood pressure.[46] To elucidate the question of the possible preventive effect of vitamin D intake in the development of hypertension, Forman et al.[47] recently evaluated dietary vitamin D intake and risk of hypertension from three large, prospective cohort studies comprising over 200,000 participants from the Nurses' Health Studies and the Health Professionals Follow-up Study, but found no relationship. However, given the importance of sun exposure and other factors in addition to dietary vitamin D intake as determinants of vitamin D status, it is unclear whether apparent differences in reported vitamin D intake accurately reflected important differences in vitamin D status, particularly the ability to identify individuals with suboptimal vitamin D status, who would be those most likely to manifest any hypertensive effects associated with vitamin D status. Thus, considering the potential limitations of the studies, future prospective studies investigating biomarkers of vitamin D insufficiency and the risk of incident hypertension are needed.

Dyslipidemia, Proinflammatory and Prothrombotic State

Dyslipidemia and a proinflammatory-prothrombotic state are components of the metabolic syndrome. There is compelling evidence that vitamin D status, and specifically 1,25-dihydroxyvitamin D, can affect cytokine production and immunity. The hormonal form of vitamin D can inhibit the production of proinflammatory cytokines, including interleukin (IL)-1, IL-2, IL-6, tumor necrosis factor-α, and others, likely via the vitamin D receptor expressed in monocytes and activated T lymphocytes.[48] Although it is well known that vitamin D plays a role in immunity, there is little evidence that vitamin D status is connected to the proinflammatory or prothrombotic components of the metabolic syndrome. Low circulating 25-hydroxyvitamin D levels have been noted in some patients with cardiovascular disease and dyslipidemia,[49,50] and hypovitaminosis D has been associated with increased total serum cholesterol concentration.[38,51] There is little mechanistic evidence, however, suggesting a likely mechanism by which vitamin D status could affect the development of dyslipidemia.

CONCLUSIONS

Increasing awareness of the prevalent nature of the metabolic syndrome and the rising number of cases of type 2 diabetes in the wake of the "obesity epidemic" has focused increased attention on the identification of potentially modifiable risk factors. Poor vitamin D status has been connected with suboptimal insulin responsiveness in both animal and human studies. Vitamin D

insufficiency and deficiency are common in some population groups. Additional scientific scrutiny of the role of vitamin D status on insulin sensitivity and glucose homeostasis and the possible benefits of increased vitamin D intake in various populations seems warranted.

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