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Vitamin D and Depression: Where is all the Sunshine?

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Abstract

Depression in its own right is a disabling condition impairing all aspects of human function. In persons with a chronic medical disease, depression often makes the management of chronic illness more difficult. Recently, vitamin D has been reported in the scientific and lay press as an important factor that may have significant health benefits in the prevention and the treatment of many chronic illnesses. Most individuals in this country have insufficient levels of vitamin D. This is also true for persons with depression as well as other mental disorders. Whether this is due to insufficient dietary intake, lifestyle (e.g., little outdoor exposure to sunshine), or other factors is addressed in this paper. In addition, groups at risk and suggested treatment for inadequate vitamin D levels are addressed. Effective detection and treatment of inadequate vitamin D levels in persons with depression and other mental disorders may be an easy and cost-effective therapy which could improve patients' long-term health outcomes as well as their quality of life.

Depression is the leading cause of disability worldwide, affecting about 121 million people (World Health Organization [WHO], 2008). In the United States, 14.8 million (or about 6.7%) adults have depression. Depression is the leading cause of disability for Americans between the ages of 15 and 44 (National Institutes of Mental Health [NIMH], 2008). Currently, the WHO has determined that depression is ranked fourth on the global burden of disease list. The rates of depression continue to increase and the WHO predicts that it will be the second most common global burden of disease by the year 2020. Depression costs $36.6 billion and 225 million lost workdays each year in the United States (NIMH, 2006).

DEPRESSION TREATMENT CONSIDERATIONS

Common treatments for depression include antidepressant medication and psychotherapy. Treatment for depression has been found to be successful 60 to 80% of the time; however, fewer than 25% of people with depression receive treatment (WHO, 2008). When treatment is not successful, it is usually related to non-compliance with medication. Patients discontinue their medication due to unwanted side effects, financial reasons, fear of

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addiction, and the belief that the medication is no longer necessary. It has been reported that 42.4% of patients discontinue medication within 30 days of initiating treatment and 52.1% of patients discontinue medication within 60 days (Olfson, Marcus, Tedeschi, & Wan, 2006).

Depression is considered a chronic or recurrent condition. People with a history of three prior episodes of major depression have a relapse rate of 70 to 80% and people with no prior history have a relapse rate of 20 to 30% (Segal, Pearson, & Thase, 2003). In addition, persons who have less than an 85% adherence to the recommended medication treatment plan are at great risk for relapse (Thase, 2003). Due to the high rate of patient medication discontinuation as well as the high rates of relapse, it is important to consider other factors that can be targeted to treat depression. One important factor needing examination is nutrition, particularly dietary supplements.

Evidence-based nutritional recommendations for persons with depression and other mental disorders have not been determined. Recently, Lakhan and Vieria (2008) reported on proposed nutritional deficiencies and treatments for persons with major depression, bipolar disorder, schizophrenia, and obsessive compulsive disorder (Table 1). Others have reported on the association between depression and inadequate intakes of some selected nutrients such as folate (Murakami et al., 2008; Payne et al., 2008), vitamin B12 (Sanchez-Villegas et al., 2009), as well as selenium, iron, and zinc (Bodnar & Wisner, 2005). In addition, intake of certain fatty acids suggests a possible beneficial effect on some mental disorders (Sanchez-Villegas et al., 2007), and for treatment of depressive symptoms in middle-aged women (Lucas, Asselin, Merette, Poulin & Dodin, 2009). Although vitamin D has recently gained widespread interest, little information relative to its impact on mental disorders is available.

It has been estimated that over one billion people have either vitamin D insufficiency or deficiency (Holick, 2007). The best assessment of vitamin D is by a serum 25-hyroxyvitamin D (25-OH D) level (Holick, 2006). Vitamin D deficiency is defined as a level less than 20 ng/mL and vitamin D insufficiency is a level less than 30 ng/mL (Holick, 2007). The impact that vitamin D may have on disorders such as cancer, osteoporosis, cardiovascular disease, and, more recently, diabetes has been reported (Holick, 2007; Lee, O'Keefe, Bell, Hensrud, & Holick, 2008; Penckofer, Kouba, Wallis, & Emanuele, 2008; Pittas, Lau, Hu, & Dawson-Hughes, 2007; Wallis, Penckofer, & Sizemore, 2008). Berk et al. (2007) reported that vitamin D deficiency may play a role in depression and possibly other mental disorders. In addition, they suggested that it could play a role in the supplementary treatment of depression. Another recent report summarized studies on vitamin D and mood disorders in women, suggesting that vitamin D may be an important nutrient for women's physical and mental well being (Murphy & Wagner, 2008).

RELATIONSHIPS BETWEEN VITAMIN D AND DEPRESSION AND OTHER MENTAL HEALTH DISORDERS

There has been research examining the relationship of vitamin D to seasonal affective disorder (SAD), schizophrenia, and depression. Several studies have examined whether light therapy improved mood. Partonen, Vakkuri, Lamberg-Allardt, and Lonnqvist (1996) randomized 29 patients (16 with SAD and 13 controls) in a parallel fashion to either one hour or 15 minutes of light therapy in the morning for two weeks in the winter. One hour of light therapy significantly decreased depressive symptoms more so in the group with SAD than the control group (p = .003). Gloth, Alam, and Hollis (1999) randomized 15 participants with SAD to either 100,000 IU of vitamin D (one time dose) (n = 8) or phototherapy (n = 7). They reported that depression (assessed with the Hamilton Depression

Scale) decreased in persons who received vitamin D (from 10.9 to 6.2, $p = .040$) as compared to those who received phototherapy (from 12.6 to 11.3, p = ns). There were no untoward side effects from the dose of vitamin D; however, a limitation of the study was the one time dose.

Studies have examined the relationship of vitamin D to other psychiatric disorders. In a prospective birth cohort that studied the intake of vitamin D supplements in the first year of life, it was noted that an intake of 2,000 IU or more per day was associated with a reduced risk of developing schizophrenia (RR = 0.23, CI = .06–.95) for males. The limitations of the study were that although there was a large sample (over 9,114 persons), the number of individuals with schizophrenia was small ($n = 79$) (McGrath et al., 2004). In addition, exposure to vitamin D was based on the mother's self-report in the first year of life. Lower levels of vitamin D have been noted with other mental disorders. Schneider, Weber, Frensch, Stein, and Fritze (2000) reported that vitamin D levels were lower in persons with schizophrenia (Mean = 35.1 pg/ml) and major depression (37.3) when compared to healthy controls (45.9). However, the difference was lower only for those with schizophrenia when compared to the controls ($p < .02$).

For other groups, the relationship of vitamin D and mood has been explored. In a cross sectional study of 80 older adults (40 mild Alzheimer and 40 nondemented), aged 60 to 92, more than half (58%) were noted to have vitamin D levels that were abnormally low. In addition, vitamin D deficiency was associated with the presence of an active mood disorder as assessed by the depressive symptoms inventory (Odds ratio: 11.69, $p = .022$) (Wilkins, Sheline, Roe, Birge, & Morris, 2006). Interestingly, vitamin D category (sufficient, insufficient, and deficient) was not predictive of Alzheimer disease. For persons with the chronic illness of fibromyalgia ($n = 75$), 69% were noted to have deficient or insufficient levels of vitamin D. Depression was higher (assessed with the Hospital and Anxiety Depression Scale [HADS] Median = 31) for those individuals with vitamin D deficiency when compared to those with insufficient (HADS = 22.5) or normal (HADS = 23.5) levels of vitamin D (Armstrong et al., 2007). Finally, it has been reported that for persons with secondary hyperparathyroidism ($n = 21$), lower serum vitamin D was significantly related to higher scores on the Beck Depression Inventory when compared to controls ($n = 63$, $p <.05$) (Jorde, Waterloo, Saleh, Haug, & Svartberg, 2006).

Recently, Hoogendijk et al. (2008) reported in a population-based cohort study of over 1,200 persons aged 65 and older, that levels of 25 (OH) D were 14% lower in persons with minor depression and 14% lower in persons with major depressive disorder when compared to controls ($p < .001$). The Center for Epidemiologic Studies-Depression (CES-D) scale was used to assess for depression, and persons also had a psychiatric evaluation using the Diagnostic Interview Schedule to verify their mental status. Depression severity was associated with low serum 25 (OH) D ($p < .001$), even after adjustment for age, sex, body mass index, smoking status, and the number of chronic conditions ($p = .01$).

The mechanism whereby vitamin D may be associated with mental disorders is not clearly understood. It has been reported that there are vitamin D receptors in the hypothalamus, which may be important in neuroendocrine functioning (Eyles, Smith, Kinobe, Hewison, & McGrath, 2005). Some investigators have reported that vitamin D is important for brain development (Eyles, Brown, Mackay-Sim, McGrath, & Feron, 2003; McCann & Ames, 2008). Eyles et al. (2003) reported that when rats were born to vitamin D deficient mothers, this negatively affected the development of their brain in terms gross morphology, cellular proliferation, and growth factor signaling. They also had decreased expression of nerve growth factor. Although these types of changes have been noted in the brains of persons with schizophrenia-like disorders, they cautioned against drawing a strong inference since more research is needed to examine the long term consequences of vitamin D depletion on the brain.

EFFECTS OF VITAMIN D SUPPLEMENTATION ON MENTAL AND PHYSICAL WELL BEING

The use of vitamin D supplementation has been examined for its effects on mood outcomes, particularly in healthy persons. In one study (Harris & Dawson-Hughes, 1993), 250 healthy women were randomized to daily vitamin D (400 IU) or a placebo for a period of one year. Both groups received supplemental calcium during the trial. Findings indicated no difference in mood scores (Profile of Mood States) between the two groups. In addition, changes in vitamin D levels were not correlated to changes in mood scores. Results suggested that the dose of vitamin D may have been insufficient to cause a significant treatment difference between groups. Lansdowne and Provost (1998) randomly assigned 44 healthy persons to varying doses of vitamin A plus one of the following: 400 IU of vitamin D/day or 800 IU of vitamin D/day, or a placebo for a period of five days. The Positive and Negative Affect Scale was used to assess mood at the end of the five days. Results showed enhanced positive affect for the vitamin D treatment groups when compared to the placebo group ($p < .001$). In addition, although both vitamin D treatment groups experienced a reduction in negative affect when compared to the placebo group, it was not statistically significant. Although the study demonstrated positive benefits in persons who were healthy, the effect on persons with depression or mood problems was not explored.

Kenny, Biskup, Robbins, Marcella, and Burleson (2003) used a randomized trial to determine the benefit of cholecalciferol (1000 IU of D_3) or a placebo in elderly men (65 to 87). All patients received supplemental calcium. Results indicated that there was no effect on general, physical, and mental health outcomes. However, men who participated in the study were in excellent health and did not have vitamin D deficiency. Therefore, this may have affected the ability to detect a significant treatment effect. However, a relationship between vitamin D levels and mental health outcomes was found ($r = 0.30$, $p = .025$). Vieth, Kimball, Hu, and Walfish (2004) conducted a randomized trial that examined the effect of vitamin D supplementation on well being. Well being was measured using a brief questionnaire based on conventional depression screening tools. One group of patients ($n = 33$) received 600 IU per day while the other group ($n = 33$) received 4000 IU per day for three months. A significant improvement in well being over time in both groups was noted following treatment (December to February) ($p < .012$). Although the group receiving the higher dose had a greater response than the lower dose group, the difference was not statistically significant.

More recently, the effect of vitamin D supplementation on symptoms of depression in overweight and obese persons was studied (Jorde, Sneve, Figenschau, Svartberg, & Waterloo, 2008). For participants who participated in this clinical trial, they were randomized into one of three groups where vitamin D (20,000 IU cholecalciferol) was given twice per week, once per week, or not at all (placebo) for one year. All participants also received calcium supplementation (500 mg daily). Findings indicated that for the two groups that received vitamin D, there was a significant improvement in depression (using the Beck Depression Inventory) which was more pronounced in those with higher depression at baseline. Limitations of the study were that only overweight and obese adults were included, and participants did not have to have depression at baseline to participate.

Research indicates that vitamin D may improve many health outcomes, particularly cancer and osteoporosis (Bischoff-Ferrari, 2007; Bouillon et al., 2006; Holick, 2007). A meta-analysis of randomized, controlled trials for vitamin D noted that intake of ordinary supplemental doses of vitamin D (from 300 IU to 2000 IU) was associated with a reduced risk of mortality (RR = 0.93, CI = 0.87–0.99) (Autier & Gandini, 2007). However, a recent report by the Agency for Healthcare Research and Quality (2009), which included 165 primary articles and 11 systematic reviews, reported that because of significant differences in the quality of the studies conducted, findings regarding vitamin D, calcium, or both nutrients on various health outcomes were inconsistent, and determining a dose-response relationship was difficult. For that reason, future placebo-controlled randomized trials will need to be conducted to examine the benefit of vitamin D supplementation on health outcomes targeted at life stages.

THE IMPACT OF SUNLIGHT ON VITAMIN D STATUS

Assessment of vitamin D status will need consideration of other factors, such as light therapy and sun exposure. Exposure to sunlight accounts for over 90% of the vitamin D requirement for most individuals (Holick, 2004). Amount of exposure to ultraviolet B radiation is affected by latitude, season, and time of the day. It has been reported that sun exposure is greatest in spring to early fall and during sunlight hours (Holick, 2004). Although places closer to the equator have greater sun exposure (Hawaii, Arizona, Florida), recently it has been reported that in even in these areas vitamin D insufficiency persists (Binkley et al., 2007; Jacobs et al., 2008; Levis et al., 2005). Since it is possible that persons who are outdoors may be more physically active, it is important to consider whether sunshine alone or in combination with physical activity is related to improved mood.

Light therapy and exercise are two well known alternative treatments to depression. However, there are few studies that demonstrate a benefit from combining the two together. In one study, 98 participants were randomized to one of three groups: (a) aerobic training program in bright light, (b) aerobic training program in normal light, or (c) stretching/relaxation program in bright light (Leppamaki, Partonen, Hurme, Haukka, & Lonnqvist, 2002). There was an improvement in depression scores (p = .05) and atypical symptoms of depression (carbohydrate craving, weight gain, social avoidance, increased appetite, fatigue, afternoon slump, and increased need for sleep) (p = .02) for those exposed to bright light. Although people who exercised in normal light had an improvement in depression (p = .02), there was no significant improvement in the atypical symptoms of depression. Therefore, the bright light may be important for improvement of atypical depression symptoms.

It may be beneficial to exercise outdoors with increased exposure to natural sunlight. A tri-modal intervention (LEVITY) which targeted mood and included (1) a brisk 20-minute outdoor walk five days per week, (2) increased light exposure, and (3) a special vitamin regimen (thiamine, pyroxidine, riboflavin, folic acid, selenium, and vitamin D), was tested in healthy women, aged 19 to 78, who reported mild to moderate depressive symptoms (scores between 11 and 29 on the CES-D) (Brown, Goldstein-Shirley, Robinson, & Casey, 2001; Brown & Shirley, 2005). Women were randomized to the treatment group (n = 53) or the control group (who only received placebo vitamins) (n = 51) and received the intervention for eight weeks. Both groups improved over time on all measures. Although the control group scores were worse at baseline despite the randomization, after controlling for baseline differences, the improvement in mood, overall well being, self esteem, happiness, and depression was significantly greater in the group that received the tri-modal intervention.

Mind, a charity group in the United Kingdom, has recommend Ecotherapy as a treatment to depression. Ecotherapy involves exercising outdoors instead of inside a facility. A research study was done with 20 people each walked outside and at an indoor shopping center (Mind, 2007). Participants then rated their feelings of self-esteem, depression, and tension after both walks. Improvements were greater when walking outdoors as compared to walking indoors (self-esteem: 90% vs. 17%, depression: 71% vs. 45%, and tension: 71% vs. 28%, respectively) (Mind, 2007). Lack of information regarding specific measurements and methods used for data collection are significant limitations of this report.

Exercise involving exposure to natural sunlight is a new development in alternative treatment to depression. Combining exercise and light therapy can easily be accomplished by encouraging people to exercise outdoors during daylight hours. However, the benefit of exercise with natural sunlight exposure needs to be weighed against the risk of skin cancer if sun exposure is significant. Therefore, additional research is needed in this area.

IMPACT OF OTHER FACTORS ON VITAMIN D STATUS

Individuals obtain vitamin D either exogenously, from dietary sources, or endogenously, from activation of a subcutaneous vitamin D precursor by ultraviolet rays (Holick, 2006). Dietary sources can be obtained through (a) naturally-occurring vitamin D in foods, (b) fortification of foods with vitamin D, and (c) a vitamin D supplement. As vitamin D is a fat-soluble nutrient, metabolism requires normal digestion and absorption of fat. Subcutaneous synthesis is stimulated by exposure to sunlight though this effect varies based on the amount and duration of exposure, latitude, season, and race (Centers for Disease Control and Prevention [CDC], 2008).

Optimal vitamin D status is hampered by several factors. The limited number of naturally rich foods with this nutrient causes some groups to be at risk for inadequacy (Whiting & Calvo, 2006). The optimal daily requirement for various age groups is under scientific debate (CDC, 2008). The current Adequate Intake (AI), which is part of the Dietary Reference Intakes (DRIs), is 200 IU/day for both women and men from infancy to age 50; 400 IU/day for those between 51–70 years; and 600 IU/day for those >70 years (Otten, Hellwig, & Meyers, 2006). Recently, the American Academy of Pediatrics recommended increasing the daily intake of vitamin D to 400 IU/day for all infants, children, and adolescents (Wagner, Green, & the Section on Breast Feeding and Committee on Nutrition, 2008).

Effective methods to ensure adequate nutrient delivery for all age groups are an issue. Vieth (1999) has suggested a range of 800–1,000 IU/day for elderly individuals and possibly even as high as 4,000 IU/day for some. Heaney (2000) recommends 1,000 IU/day routinely for elderly patients seen in an osteoporosis clinic. Other reports have suggested that optimal oral D_3 intake be in the range of 400–1,600 IU/day with individual variation possibly due to adipose mass and other metabolic conditions (Arunabh, Pollack, Yes, & Aloia, 2003; Dawson-Hughes et al., 2005; Heaney, 2000; Wortsman, Matsuoka, Chen, Lu, & Holick, 2000). The Institute of Medicine (2009) has appointed a committee to make recommendations related to revised vitamin D DRIs. This is important as current recommendations are based on the amount needed to prevent rickets (Cashman, 2007; Cashman et al., 2008; Vieth et al., 2007; Whiting & Calvo, 2005).

ASSESSMENT AND GROUPS AT RISK FOR LOW VITAMIN D

The signs and symptoms of vitamin D deficiency vary depending on the age and severity. For children, there has been a reappearance of rickets from vitamin D deficiency. Symptoms of rickets can vary and may include bone pain, delayed tooth eruption, and poor growth (Misra et al., 2008). Deficient adults may experience muscle weakness, bone pain, difficulty walking, and frequent falls (Holick 2007; Powell & Greenberg, 2006). Persons more at risk for vitamin D include those with malabsorption syndromes such as inflammatory bowel disease, celiac disease, and chronic diarrhea (Wallis, Penckofer, & Sizemore, 2008).

Other factors may influence the availability and metabolism of this nutrient. Thus, various population groups have been identified as high risk for vitamin D insufficiency or deficiency. Those with limited sun exposure, due to being homebound, living in latitudes >34° north or south, and/or clothing that covers most of the body, are at risk for vitamin D deficiency (Office of Dietary Supplements [ODS], 2009). Similarly, older adults are often at risk of vitamin D inadequacy. This is due to reduced subcutaneous production and intestinal absorption (Whiting & Calvo, 2005). When coupled with limited sun exposure, which is the case for many older adults, the risk increases (Heaney, 2006).

Findings from the National Health and Nutrition Examination Survey (NHANES-III, 1988–1994), which included more than 15,000 adults, indicated significantly lower levels of vitamin D for female than male participants. In addition, vitamin D levels were highest in whites, followed by Hispanics and then African Americans (Zadshir, Tareen Pan, Norris, Martins, 2005). More recent findings from NHANES (2001–2004) have indicated that these differences race continue to exist for vitamin D insufficiency (Ginde, Liu, & Camargo, 2009). For individuals who have darker skin, decreased vitamin D is more common. Due to higher melanin levels, dark-skinned individuals experience reduced subcutaneous vitamin D synthesis compared to those with lighter pigmentation, making them another high risk group for vitamin D deficiency (Harris, 2006).

For infants, breast feeding is highly recommended; however, human milk is a poor source of vitamin D, making deficiency a concern for breast-fed infants. The American Academy of Pediatrics recommends that infants who are solely or partially breast-fed receive 400 IU/day of vitamin D within the first few days until consuming adequate amounts of another vitamin D fortified formula or whole milk (Wagner et al., 2008).

In healthy adolescents, vitamin D deficiency has been noted as a common finding in the United States and abroad (Das, Crocombe, McGrath & Mughal, 2006; Gordon, DePeter, Feldman, Grace, & Emans, 2004). Similar to findings for adults, African American adolescents and girls experience a higher prevalence of vitamin D deficiency than white or Asian adolescents and boys (Gordon et al., 2004). Dietary habits inversely related to vitamin D deficiency were consumption of milk and ready-to-eat cereals; whereas soda, juice, and iced tea intake were positively correlated to vitamin D deficiency (Gordon et al., 2004). Adolescents also may be prone to vitamin D deficiency because of obesity.

Obesity has been found to be inversely related to vitamin D level (Arunabh et al., 2003; McGill, Stewart, Lithander, Strik & Poppitt, 2008; Wortsman, Matsuoka, Chen, Lu, & Holick, 2000). This may be due to excess adipose tissue that sequesters vitamin D thereby altering its release into circulation (Wortsman et al., 2000). Body image concerns may also cause obese individuals to avoid skin exposure to the sun resulting in inadequate vitamin D levels (McGill et al., 2008). Obesity is associated with insulin resistance, and there is evidence to suggest that vitamin D may be important in the prevention of diabetes (Pittas, Lau, Hu, & Dawson-Hughes, 2007). There is also evidence to suggest that vitamin D may be important in the treatment and prevention of complications associated with diabetes (Penckofer et al., 2008).

TREATMENT AND PRACTICE IMPLICATIONS FOR INADEQUATE VITAMIN D

Sunshine has been suggested as an approach to maintain healthy vitamin D levels. Holick (2004) reported that sun exposure to the arms and legs for five to ten minutes, two or three times per week, may be beneficial for maintaining vitamin D sufficiency. However, because the time of day, season, and latitude influence sunlight absorption and thus, the amount of vitamin D produced, it becomes difficult to make universal recommendations. In addition, because the risk of skin cancer is associated with unprotected sun exposure, it is usually not recommended for treatment of inadequate vitamin D levels.

Nutritional sources of vitamin D are limited. Two forms of vitamin D are found in foods naturally (Holick, 2007). Certain fatty fish, fish oils, and eggs are some of the richest sources of Vitamin D_3, or cholecalciferol without fortification. Vitamin D_2, or ergocalciferol, is found in some mushrooms. Vitamin D content of foods is lacking in commonly used databases (Holden & Lemar, 2008). The USDA Nutrient Data Laboratory is currently collaborating with experts to update existing information including evaluation of optimal analytical methods (Holden, 2008). Table 2 summarizes both naturally-occurring and fortified food sources of vitamin D based on currently available information. It is anticipated that these resources will be expanded in the near future.

In the United States, vitamin D fortification is required for nonfat dry and evaporated milk, and is optional, but common, for fluid milk at a maximum level of 400 IU/quart (Rover & O'Brien, 2008). Other foods with optional fortification status and that are commonly available are many ready-to-eat cereals, and some juices, yogurt, farina, pastas, and margarines (Rover & O'Brien, 2008). Because only some foods are fortified with vitamin D, and since food manufacturers frequently change product formulations, including vitamin fortification, patients should be encouraged to read the nutrition facts label on a regular basis in making food choices. The success of food fortification in treating other diseases, namely pellagra with niacin and neural tube defects with folate, has lead to consideration of enhanced vitamin D food fortification. This might include expanded optional and/or mandatory fortification (similar to folate in grain products) (Vieth et al., 2007; Whiting & Calvo, 2006). Since cheese is commonly used in foods prepared at and away from home, food scientists are in the process of developing ways to use this popular food as a new source of vitamin D fortification (Johnson et al., 2005). While interesting options for food fortification are being investigated, the most effective or acceptable strategies have not been determined.

For many persons, sunshine or diet alone will not be sufficient in providing adequate amounts of vitamin D. There is evidence to suggest that supplementation may be necessary. Supplemental doses that provide the AI (400–600 IU vitamin D/day) result in small increases in serum 25 (OH) D levels but may not be adequate to correct deficiency in a timely manner or optimize vitamin D nutrition (Talwar, Aloia, Pollack, & Yeh, 2007; Vieth et al., 2007). Holick recommends a standard supplementation protocol for non-pregnant adults to treat vitamin D deficiency using a two-phase protocol. The initial phase is a single 50,000 IU vitamin D_2 capsule weekly, for eight weeks (Holick, 2007). After the initial phase, serum 25 (OH) D levels should be evaluated and ideally be >30 ng/ml. If this minimal serum level has not been achieved, then the initial phase may need to be repeated. The second phase is a 50,000 IU vitamin D_2 capsule every one to four weeks ongoing.

In African American post-menopausal women, Talwar et al. (2007) developed an algorithm of vitamin D_3 supplementation to achieve optimal serum concentrations. They suggested a dose of 2,800 IU/d if serum 25 (OH) D was >18 ng/ml or 4,000 IU/d if serum 25 (OH) D was <18 ng/ml. Correction of deficiency may vary in those with malabsorption and/or nephrotic syndromes, obesity, or medication use that activates steriod or xenobiotic receptors (Holick, 2007). Hyperparathyroidism or granulomatous disorders also require special consideration in treating vitamin D deficiency. Specific vitamin D recommendations for those with diabetes, with or without vitamin D deficiency, have yet to be determined (Pittas et al., 2007).

Discussions of revised recommendations are often accompanied by cautionary words related to prevention of toxicity (Heaney, 2000). Clinical manifestations of vitamin D toxicity include nonspecific symptoms of nausea, vomiting, poor appetite, constipation, and weakness (ODS, 2009). Vitamin D toxicity is an elevated vitamin D level greater than 150 ng/dl. The normal upper limit has been considered to be 55 to 60 ng/ml, but is being re-evaluated as levels up to 125 ng/dl have been reported without adverse effects (Holick, 2006). Serum calcium levels should be monitored with administration of vitamin D as toxicity is associated with hypercalcemia which may cause mental status changes and irregular heart rhythms (ODS, 2009). Therefore, treatment of deficiency and supplementation should be coupled with appropriate medical supervision and monitoring.

SUMMARY

As previously discussed, those groups who are at risk for vitamin D deficiency include the elderly, adolescents, obese individuals, and those with chronic illnesses (e.g., diabetes). Interestingly, it is these same groups that have also been reported to be at risk for depression (CDC, 2009; Lemstra et al., 2008; Lustman, Penckofer, & Clouse, 2008; Strine et al., 2008). The role that vitamin D supplementation could play in the prevention and treatment of depression has not been studied and should be an important area of future research. If exercising outdoors in the sunshine, eating foods rich in vitamin D, and/or taking dietary supplements to improve vitamin D deficiency could improve one’s mental well being, it would be a simple and cost-effective solution for many who are at risk for depression and possibly other mental disorders.

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TABLE 1

Mental Disorders and Alternative Treatments

Mental Disorder	**Proposed Cause**	**Treatment**
Major Depression	Serotonin deficiency	Tryptophan
	Dopamine/Noradrenaline deficiency	Tyrosine
	GABA deficiency	GABA
	Omega-3 deficiency	Omega-3s
	Folate/Vitamin B deficiency	Folate/Vitamin B
	Magnesium deficiency	Magnesium
	SAM deficiency	SAM
Bipolar Disorder	Excess acetylcholine receptors	Lithium orotate & taurine
	Excess vanadium	Vitamin C
	Vitamin B/Folate deficiency	Vitamin B/Folate
	L-Tryptophan deficiency	L-Tryptophan
	Choline deficiency	Lecithin
	Omega-3 deficiency	Omega-3s
Schizophrenia	Impaired serotonin synthesis	Tryptophan
	Glycine deficiency	Glycine
	Omega-3 deficiency	Omega-3s
Obsessive Compulsive Disorder	St. John’s Wort deficiency	St. John’s Wort

Note: Adapted with permission from Lakhan, S. E., & Viera, K.F. (2008). Nutritional therapies for mental disorders. *Nutrition Journal*, 7(2): doi: 10.1186/1475-2891-7-2.

GABA = gamma-aminobutyric, SAM = S-adenosylmethionine

TABLE 2

Vitamin D Content of Selected Foods

Food Item	Amount	Vitamin D (mcg)	Vitamin D (IU)	% Daily Value*	Source
Herring, Atlantic	100 gm	40.7	1,628	407	Weihrauch
Salmon, canned, pink	100 gm	15.6	624	156	Weihrauch
Halibut, Greenland	100 gm	15.0	600	150	Weihrauch
Catfish, channel	100 gm	12.5	500	125	Weihrauch
Tuna, light meat, canned in oil	100 gm	5.9	236	59	Weihrauch
Yoplait yogurt, regular or light	6 oz = 170 gm	2.0	80	20	www.yoplait.com
Orange juice, vitamin D fortified	100 gm	1.4	57	14	USDA National Nutrient Database, Release, 21
Egg, chicken, whole	100 gm	1.3	52	11	Weihrauch
Milk, cow, whole, vitamin D fortified	100 gm	1.0	40	10	Weihrauch
Milk, cow, 2%, vitamin D fortified	100 gm	1.0	40	10	Weihrauch
Milk, cow, skim, vitamin D fortified	100 gm	1.0	40	10	Weihrauch
Cereals, ready-to-eat, fortified**	varies approx 1 cup (25–30 gm)	1.0	40	10	Product info—see below
Soymilk, lowfat, fortified with calcium, vitamins A and D	100 gm	1.0	41	10	USDA National Nutrient Database, Release, 21
Milk, goat, whole	100 gm	.3	12	3	Weihrauch
Cheeseburger	100 gm	.3	12	3	Weihrauch
Milk, human, whole, fluid	100 gm	.09	4	1	Weihrauch

* Based on a Daily Value = 400 IU for adults and children older than 4 years old. Food labels are not required to list vitamin D content unless fortified.

** Examples of ready-to-eat cereals fortified with vitamin D include: Corn Chex®, Cherrios®, Wheaties®, Special K®, Product 19®, and Corn Flakes®. Many others are available and identified by reading the nutrition facts labels on food packages.

General Mills product information retrieved February 4, 2009, from http://www.generalmills.com/corporate/brands/brand.aspx?catID = 50amp;groupID = 19412

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Yoplait product information retrieved February 4, 2009, from http://www.yoplait.com/products_original.aspx mcg = microgram, IU = International Unit, 1 mcg = 40 IU