Breakthrough Updates You Need to Know on Vitamin D

The compound we call vitamin D can no longer properly be considered a vitamin. For most mammals, it is not in any sense even a nutrient. Nevertheless, vitamin D resembles true vitamins inasmuch as humans -- who are cut off from the critical solar ultraviolet wavelengths by reason of latitude, clothing, or shelter -- depend on an external source of the substance, just as they do for the true essential nutrients.

What is Vitamin D?

Vitamin D, calciferol, is a fat-soluble vitamin. It is found in food, but also can be made in your body after exposure to ultraviolet rays from the sun. Vitamin D exists in several forms, each with a different activity. Some forms are relatively inactive in the body, and have limited ability to function as a vitamin. The liver and kidney help convert vitamin D to its active hormone form.

The major biologic function of vitamin D is to maintain normal blood levels of calcium and phosphorus. Vitamin D aids in the absorption of calcium, helping to form and maintain strong bones. It promotes bone mineralization in concert with a number of other vitamins, minerals, and hormones.

Without vitamin D, bones can become thin, brittle, soft, or misshapen. Vitamin D prevents rickets in children and osteomalacia in adults, which are skeletal diseases that result in defects that weaken bones.

What are the sources of vitamin D?

Food sources

Fortified foods are the major dietary sources of vitamin D. Prior to the fortification of milk products in the 1930s, rickets (a bone disease seen in children) was a major public health problem in the United States. Milk in the United States is fortified with **10 micrograms (400 IU) of vitamin D per quart,** and rickets is now uncommon in the US.

Exposure to sunlight

Exposure to sunlight is an important source of vitamin D. Ultraviolet (UV) rays from sunlight trigger vitamin D synthesis in the skin.

Season, latitude, time of day, cloud cover, smog, and suncreens affect UV ray exposure. For example, in Boston the average amount of sunlight is insufficient to produce significant vitamin D synthesis in the skin from November through February.

Sunscreens with a sun protection factor of 8 or greater will block UV rays that produce vitamin D.

Vitamin D supplements are often recommended for exclusively breast-fed infants because human milk may not contain adequate vitamin D.

Vitamin D and Bone Health

It is estimated that over 25 million adults in the United States have, or are at risk of developing osteoporosis. Osteoporosis is a disease characterized by fragile bones. It results in increased risk of bone fractures.

Rickets and osteomalacia were recognized as being caused by vitamin D deficiency 75 years ago; their prevention and cure with fish liver oil constituted one of the early triumphs of nutritional science. The requirement for vitamin D has been pegged to these disorders ever since.

Having normal storage levels of vitamin D in your body helps keep your bones strong and may help prevent osteoporosis in elderly, non-ambulatory individuals, in post-menopausal women, and in individuals on chronic steroid therapy.

Researchers know that normal bone is constantly being remodeled (broken down and rebuilt). During menopause, the balance between these two systems is upset, resulting in more bone being broken down (resorbed) than rebuilt.

Vitamin D deficiency has been associated with greater incidence of hip fractures. A greater vitamin D intake from diet and supplements has been associated with less bone loss in older women. Since bone loss increases the risk of fractures, vitamin D supplementation may help prevent fractures resulting from osteoporosis.

The use of vitamin D is well accepted, but the mere absence of clinical rickets can hardly be considered an adequate definition either of health or of vitamin D sufficiency.

The fact that it takes 30 or more years to manifest itself makes it no less a deficiency condition than a disorder that develops in 30 days. It is easy to understand how long-period deficiency diseases could never have been recognized in the early days of nutritional science, but with modern methods and a better grasp of the relevant physiology, failing to recognize a slowly developing condition as a true deficiency state, can no longer be justified.

Vitamin D nutrition probably affects major aspects of human health, as listed below, other than its classical role in mineral metabolism. The rest of the article addresses some of the newly recognized uses of vitamin D.

Cancer

Today, it is well established that besides playing a crucial role in the establishment and maintenance of the calcium in the body, the active form of vitamin D also acts an effective regulator of cell growth and differentiation in a number of different cell types, including cancer cells.

Laboratory, animal, and epidemiologic evidence suggest that vitamin D may be protective against some cancers. Clinical studies now show vitamin D deficiency to be associated with four of the most common cancers:

- Breast (23)
- Prostate 24-27
- Colon 28-31
- Skin 32,33

Diabetes

Vitamin D deficiency has been associated with insulin deficiency and insulin resistance. (1-3) In fact, last year it was shown that vitamin D deficiency is likely to be a major factor for the development of type one diabetes in children. (4)

Heart Disease

Insulin resistance is also one of the major factors not only leading to the cancers mentioned above, but also to the number one killer in the US, heart disease. Northern countries have higher levels of heart disease and more heart attacks occur in the winter months. (5,6)

Arthritis

Progression of degenerative arthritis of the knee and hip is faster in people with lower vitamin D concentrations (33-34)

Infertility and PMS

Infertility is associated with low vitamin D(7), and PMS has been completely reversed by addition of calcium, magnesium and vitamin D.(8)

Fatigue, Depression and Seasonal Affective Disorder

Activated vitamin D in the adrenal gland regulates tyrosine hydroxylase, the rate limiting enzyme necessary for the production of dopamine, epinephrine and norepinephrine.

Low vitamin D may contribute to chronic fatigue and depression. (9-10) Seasonal Affective Disorder has been treated successfully with vitamin D. In a recent study covering 30 days of treatment comparing Vitamin D and 2 hour daily use of 'light boxes', depression completely resolved in the D group, but not in the light box group.(11)

Autoimmune Disorders

Multiple Sclerosis, (12) Sjogren's Syndrome, rheumatoid arthritis, thyroiditis and Crohn's disease have all been linked with low vitamin D levels.

Single, infrequent, intense, skin exposure to UV-B light suppresses the immune system and causes harm.

However chronic low-level exposure normalizes immune function and enhances immune cell production. This reduces abnormal inflammatory responses such as found in autoimmune disorders, and reducing occurrences of infectious disease. (14-18)

Obesity

Vitamin D deficiency has been linked with obesity. (18, 19) Vitamin D has recently been shown to lower leptin secretion. (20) Leptin is a hormone produced by fat cells and is involved in weight regulation. It is thought that the hormone signals the brain when fat cells are "full," but exactly how the hormone controls weight is not entirely clear.

Additionally, obesity by itself probably further worsens vitamin D deficiency due to the decreased bioavailability of vitamin D(3) from skin and dietary sources, because of its being deposited in body fat. (36)

Syndrome X

Vitamin D deficiency has been clearly linked with Syndrome X. (21) Syndrome X refers specifically to a group of health problems that can include insulin resistance (the inability to properly deal with dietary carbohydrates and sugars), abnormal blood fats (such as elevated cholesterol and triglycerides), overweight, and high blood pressure.

Vitamin D and Steroids

Steroids, like prednisone, are often prescribed to reduce inflammation from a variety of medical problems. These medicines may be essential for a person's medical treatment, but they have potential side effects, including decreased calcium absorption.

There is some evidence that steroids may also impair vitamin D metabolism, further contributing to the loss of bone and development of osteoporosis associated with steroid medications. For these reasons, individuals on chronic steroid therapy should consult with their physician or registered dietitian about the need to increase vitamin D intake through diet and/or dietary supplements.

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DR. MERCOLA'S COMMENT:

I wish to express my sincere appreciation to nutritionist Krispin Sullivan for the years she researched this subject, which provided me with so much of the foundational background for this review. She is publishing the definitive resource for vitamin D later this year called Naked at Noon.

A preliminary copy of her vitamin D research is available on her web site.

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VITAMIN D SUPPLEMENTATION IN THE FIGHT AGAINST MULTIPLE SCLEROSIS

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INTRODUCTION

Many different supplements are recommended for people with MS and it is worthwhile to examine the science and logic behind any given supplement recommendation. Vitamin D, the sunshine vitamin, is not often strongly advocated for MS, although small dosages (~200-400 IU) are usually part of a total vitamin recommendation. I have recently read a number of papers on the relationship between vitamin D and MS and the best summary of this topic is by Hayes et al (1997). This information has convinced me that persons with MS could possibly significantly benefit from a substantially higher supplementation of vitamin D than is currently proposed in various self help books (e.g. Graham, 1989) or suggested by clinicians.

In this essay I will present a brief discussion of vitamin D and follow that with the scientific evidence which supports the concept that vitamin D likely plays an important role in controlling autoimmunity and MS. Such evidence consists of epidemiological data, animal experiments, immunological analyses, genetics and the results of small clinical trials which used vitamin D or a metabolite as the therapeutic agent. When all the data are considered as a whole, it becomes apparent that adequate supplementation of vitamin D may well be beneficial and, given the very low cost and safety of such a therapy, persons with MS might want to make sure they are receiving sufficient amounts each day.

The key questions of, how much vitamin D is needed, is this amount safe and how can one best obtain this amount, are also addressed. Vitamin D is a fat- soluble vitamin and can be toxic in large dosages. Thus it is very important to examine current data in regards to vitamin D safety and reasonable sources of the vitamin. In the final part of the essay, vitamin D intake is examined in an evolutionary perspective and a summary on how vitamin D fits in the overall "Paleolithic Prescription" for MS concludes the essay.

VITAMIN D

A detailed discussion of the chemistry of vitamin D is far beyond my capabilities and the scope of this essay. For those wanting such information, DeLuca and Zierold (1998) provide a very good overview of the chemistry of vitamin D and its receptor. A few points are worth mentioning to help one gain an appreciation of what vitamin D is, how it is activated in the body, and the role it plays in health and illness. The primary source of this nutrient is not from diet but rather from a chemical photolysis reaction in the skin. When UV light from the sun penetrates the epidermis, it is absorbed by a metabolite of cholesterol (7-dehyrocholestrol) which is then converted into vitamin D (calciferol). Notably Vitamin D is biologically inert and is metabolized in the liver to produce 25 (OH)D (calcidiol) which is the main form of circulating vitamin D. Although this substance is also inactive, its concentration in the blood provides a good assessment of a person's vitamin D level and the relationship of various levels of 25(OH)D to health will be discussed later. The final step in the vitamin D story is that 25(OH)D is converted to an active hormone, 1,25(OH)2D (calcitriol), in the kidneys.

The main role of vitamin D, through the actions of its metabolized hormone, calcitriol, is to regulate the amount of calcium and phosphorous in circulation. In this way it has a major impact on bone growth or lack thereof (rickets, osteoporosis) and, when most people think of vitamin D, they think of it in this context. When calcium levels are low (usually due to insufficient vitamin D and

calcium intake), the body activates the parathyroid gland, which produces PTH (parathyroid hormone). This hormone kicks starts vitamin D hormone production and helps to remove calcium from the bones to be used in more important functions. Thus a measurement of PTH also provides a good proxy for vitamin D levels in circulation. When adequate vitamin D is available there is generally no need for the body to produce PTH and serum levels of this hormone are negligible.

As will be discussed below, recent research has uncovered more roles for vitamin D besides calcium regulation. The most relevant of these functions is as an immune regulator which has obvious implications for its putative role in MS and other autoimmune diseases.

SCIENTIFIC DATA RELATING VITAMIN D TO MS

Goldberg (1974a, 1974b) first proposed the concept that vitamin D was an important factor in MS. He marshalled a variety of epidemiological data to make a case for vitamin D being a factor in the onset and progression of MS. Goldberg emphasized the conspicuous high prevalence of MS in areas which receive a relatively low amount of sunlight. Acheson et al (1960) had earlier documented this relationship between MS prevalence and sunlight with a very impressive negative correlation between MS prevalence and hours of sunshine. Goldberg (1974a) took the next step and postulated that such a close correspondence between low sunlight and MS was due to low vitamin D production in the population. Goldberg (1974a) also showed that within areas of low sunlight (e.g. Norway) differences in MS prevalence could be explained by dietary factors which affect vitamin D production. Such factors include the amount of fish eaten (increases vitamin D) and the amount of grains consumed (reduces vitamin D levels due to the action of phytates). To explain how vitamin D levels were related to MS, Goldberg (1974b) proposed that genetically susceptible individuals may need larger than normal amounts of vitamin D during myelin formation and that insufficient vitamin D during childhood might result in defective myelin which would be susceptible to breakdown in later life. Goldberg's ideas were completely ignored by medical researchers, although, as will be discussed later, he was able to organize a small clinical trial to test his concept.

Goldberg's innovative hypothesis that vitamin D is a key factor in the development of MS and for explaining the distinctive geographic variations in MS prevalence is just as attractive today as it was 26 years ago. Science started to catch up with Goldberg in the early 80s with the recognition that immune cells carry a receptor for the active hormone of vitamin D (1,25-(OH)2D) and that this hormone likely regulates immune functions (Bhalla et al, 1983).

This discovery led to ongoing research efforts which continue to uncover a number of important ways in which vitamin D hormone affects the immune system. One area of research in this regard was a number of experimental studies with mice and rats which are genetically susceptible to animal forms of autoimmune disease such as EAE (closely resembles MS). These studies showed that injections of vitamin D hormone could protect against or arrest the animal forms of MS (Lemire and Archer, 1991; Cantorna et al, 1996), type 1 diabetes (Mathieu et al, 1994), rheumatoid arthritis (Cantorna et al, 1998a) and lupus (Lemire et al, 1992). Furthermore, immunological analyses done in conjunction with these experiments revealed the following immune-regulating actions for vitamin D hormone:

1. Suppresses antibody production by B cells and the proliferation of T cells in the thymus (Yang et al, 1993).
2. Upregulates cytokines TGF-beta and IL-4. These proteins, which are produced by immune cells, act as suppressants of inflammatory T cells (Cantorna et al, 1998b).
3. Inhibits production of pro-inflammatory cytokines such as IL-1, IL-2, TNF and IFN gamma (Muller and Bendtzen, 1996) which also reduces inflamammatory reactions.
4. Interferes with T helper function and inhibits the passive transfer of cellular immunity by Th in vivo (Thomasset, 1994)

5. Inhibits the production of NO (nitric oxide) by immune cells (Garrion et al, 1997). NO has been identified as one of the most destructive products of the immune system and is an important factor in demyelination.
6. Inhibits the proliferation of activated and memory T cells (Muller and Bendtzen, 1992). Such cells are the main mediators of the inflammatory autoimmune reactions of MS.
7. Exerts immunomodulating effects in the CNS by inducing a profound downregulation of antigen expression by both infiltrating and resident antigen presenting cells (e.g. macrophages) (Nataf et al, 1996).

In summary, vitamin D hormone has numerous effects on the immune system and acts within the CNS. All of these effects have the combined result of significantly reducing inflammatory autoimmune reactions from occurring and they readily explain why vitamin D hormone is so effective in suppressing a variety of animal autoimmune diseases including EAE (animal MS) (Hayes et al, 1997).

On the basis of the impressive immunomodulating effects of vitamin D, Schwartz (1993) hypothesized that the well established reduction of MS attacks during pregnancy and their increased occurrence following pregnancy was due in part or whole to the natural large increases in production of vitamin D hormone during pregnancy and its rapid decline afterwards. Such a hypothesis seems very plausible and hopefully will be followed up.

Genetic data also implicate vitamin D in MS and Fukazawa et al (1999) demonstrated an association between vitamin D receptor genes and MS.

Vitamin D has been used as a therapeutic agent in only a few small clinical trials. Notably Goldberg helped to organize a small trial in the early 80s (Goldberg et al, 1986). Ten subjects took 5000 IU/day of vitamin D along with about 1000mg of Ca and 600mg of Mg for two years. The subjects acted as their own controls with the exacerbation rates during the trial compared with the subjects' historical rates of exacerbation. A notable decline in exacerbation rate was noted, although the small size of the trial makes the results equivocal. Despite these results and all the scientific data showing that vitamin D would be a good therapeutic agent, no follow-up, better controlled trials have ever been done for vitamin D and MS.

Rheumatoid Arthritis

A small clinical trial for RA and a vitamin D metabolite was recently done by Andjelkovic et al (1999) over a three-month time period. The results were positive: "Therapy showed a positive effect on disease activity in 89% of the patients (45% with complete remission and 45% with a satisfactory effect). Only two patients (11%) showed no improvement, but no new symptoms occurred". Another relevant study was a large-scale investigation of the effects of vitamin D supplementation in infants and the associated risk of type 1 diabetes (Eurodiab Study Group, 1999). This study clearly demonstrated that supplementation with vitamin D was associated with a decreased risk of type 1 diabetes.

In summary, a variety of data, from epidemiology, animal experiments, immunological investigations, genetics and small clinical trials indicates that vitamin D can have a suppressant effect on autoimmune reactions and help to slow autoimmune disease. Thus its use as a supplement by persons with MS or other similar autoimmune diseases, such as rheumatoid arthritis and Crohn's, seems warranted.

SUPPLEMENTATION AND SAFETY

The above scientific data suggest that it is important for persons with cell-mediated autoimmune diseases, including MS, to have sufficient intake of vitamin D. In this section the questions of, how much, where to get it and is it safe, are addressed. The best reference for the answers to these

questions is a recent, comprehensive review by Vieth (1999) entitled "Vitamin D Supplementation, 25-hydroxyvitamin D concentrations and Safety". The answers to the above questions are provided in this excellent paper and readers wanting more information than provided below are referred to it.

On the question of how much, Vieth (1999) first notes that humans evolved having a relatively large intake of vitamin D, with a naked human in Africa likely getting at least 10000 IU a day. He then reviews all the literature on intake of vitamin D and resultant levels of 25(OH)D and PTH. The key here is that when adequate levels of 25(OH)D (an intermediate metabolite of vitamin D) are circulating there is no need for the body to produce PTH (parathyroid hormone). On the basis of all the available data, Vieth (1999) concludes that it is desirable to have 100-125 nmol/litre of 25 (OH)D in circulation. Furthermore, he notes, that to achieve this amount, an intake of about 4000 IU of vitamin D a day is required. As described earlier, the main source of vitamin D is the sun and in hot climates (south of 40 N) such an intake is readily possible if an individual spends a reasonable time in the sun. However, in colder climates, like those of Canada, northern USA and northwest Europe, it is almost impossible to average 4000 IU a day because for at least six months of the year intake from the sun is negligible at best. Even during the few hot summer months an individual would have to spend considerable time in the sun to achieve the required intake.

Thus in areas of low sunlight, supplements provide a reasonable alternative for vitamin D intake. As Vieth (1999) notes "From what is known now, there is no practical difference whether vitamin D is acquired from ultraviolet exposed skin of through diet". Cod liver oil, fish and vitamin D fortified foods are the usual dietary sources used to get vitamin D. However these sources usually supply much less than 1000 IU/day and the fortified foods provide a synthetic form of vitamin D (D2) which is substantially inferior to the natural vitamin D3 (Trang et al,1998). Furthermore, because cod liver oil also contains large amounts of vitamin A, it would not be feasible to get 4000 IU of vitamin D from it because of potential problems with too much vitamin A. Fortunately there are specific vitamin D3 supplements which are usually small 1000 IU pills and a bottle of 100 costs less than $10 ($5 CDN in Calgary). This would seem to be the most reasonable source of 4000 IU a day.

Vieth (1999) also addresses the safety issue of vitamin D at length. He shows that the "no observed adverse effect level (NOAEL)" is at least 10,000 IU/day. The lowest observed adverse effect level (LAOEL) is 40,000 IU/day. Thus 10,000 IU/day is definitely safe (assuming no hypersensitivity) and 40,000 IU/day is definitely a problem. It would be next to impossible for anyone living in a northern area to get too much vitamin D from sunlight and a 4000 IU supplement. Thus such a supplementation level is safe for anyone who is not hypersensitive to vitamin D.

It must be stressed that adequate calcium and magnesium intake must accompany vitamin D supplementation as discussed by Goldberg et al (1986). Cantorna et al (1999) recently demonstrated that calcium levels strongly affect the action of vitamin D for suppressing EAE in mice. Calcium intake should be in the range of 600-900 mg/day with magnesium intake being about the same as this.

In summary, a daily intake of vitamin D of 4000 IU along with 800 mg of both calcium and magnesium are required for adequate levels of metabolized vitamin D products to be maintained in circulation. For those in low sunlight climates, such a vitamin D intake is most easily achieved with a daily supplement of 4000 IU of a vitamin D3 product.

VITAMIN D IN A PALEOLITHIC PERSPECTIVE

Eaton and Konner (1985) hypothesized that, with the advent of agriculture and the subsequent industrial and technological revolutions, consequent changes in dietary habits and major shifts in the intake of various nutrients have adversely affected human health. They suggest that these major

changes are in part responsible for a myriad of "genetic-environmental" diseases including heart disease, stroke, type 2 diabetes and various forms of cancer. As discussed in Cordain (1999) and Cordain et al (in press), this concept can be readily applied to autoimmune diseases. In this context it is useful to examine changes in vitamin D intake during the two million year evolution of human beings and how such changes are related to the rise of MS.

Humans lived in hot climates throughout most of their development and thus they experienced a relatively large intake of vitamin D from sunlight. Natural selection would have ensured that the human genome became very compatible with such an intake, estimated to be in the range of 10000 IU a day. This would have resulted in circulating concentrations of 25(OH)D of between 100 and 140 nmol/litre which can regarded as the optimal level of vitamin D. Such a concentration supplied all the vitamin D hormone required for a variety of functions including the maintenance of a strong skeletal structure and the control of autoimmune reactions induced by foreign antigens derived mainly from infectious agents. The importance of adequate vitamin D for human health is underscored by the fact that evolution produced a very simple and seemingly fail-safe method for its attainment.

As humans migrated out of Africa into temperate areas, less sun-derived vitamin D became available and daily intakes likely fell somewhat. However, because long periods were spent outside hunting and gathering, most Paleolithic people still obtained sufficient vitamin D (>4000 IU/day) and readily maintained an adequate serum concentration of 25(OH)D throughout the year.

With the advent of agriculture about 8000 years ago and the ensuing population explosion, maintaining adequate levels of vitamin D and its metabolites started to become a problem for the first time in human history. Population pressures forced humans to migrate into even more hostile areas in terms of cold climates and low sunlight. They also tended to eat less fish and spend much more time out of the sun. Significantly, two of the main foods of agriculture have an adverse effect on the action of vitamin D. Grains, which are the number one food of agriculture, contain phytate or phytic acid which counters the action of vitamin D (Willis and Fairney, 1972). Cordain (1999) also discusses the role of grain consumption in vitamin D deficiency. Goldberg (1974a) raised this point and showed that areas where grains were grown in Norway tended to have the highest rates of MS. Notably, the only common grain with a very low phytate content is rice.

Another food introduced into the human diet by agriculture is milk. Milk may also have an adverse effect on vitamin D by affecting the vitamin D receptor on cells. Perez-Maceda et al (1991) demonstrated that part of the bovine albumin protein of milk is a molecular mimic of the vitamin D receptor. Thus an immune reaction against that milk protein can potentially result in an autoimmune reaction against the vitamin D receptor. This would significantly lower the effectiveness of vitamin D hormone to bind with a variety of cells (including immune cells) and carry out its important functions.

Our modern lifestyle has only exacerbated the problem of vitamin D deficiency and large populations now inhabit low annual sunlight areas. The consumption of fish is very low in many agricultural areas where diets are completely dominated by high phytate, gluten grains and dairy products. A dominance of indoor jobs, fears of skin cancer and the use of sunscreens have reduced exposure times to sunlight further such that, even in summer, many people do not get anywhere near the required vitamin D intake from sunlight. Thus it would appear that chronic vitamin D deficiency (<100nmol/litre of 25(OH)D) in large populations which live in low sunlight climates is a Neolithic problem and is caused by a variety of lifestyles factors which greatly differ from those of the Paleolithic when adequate vitamin D was readily obtained.

Notably persons with MS tend to be at the problematic end of the deficiency spectrum (<50 nmol/litre 25(OH)D). The reasons for this higher than normal deficiency is likely multifold and includes the tendency for persons with MS to spend less time outside doing various laborious or

sporting activities, the use of steroidal drugs in treatment, diets with an abundance of grains and milk and no encouragement from their doctors or MS societies to take sufficient vitamin D supplements. A study of 80 persons with MS by Nieves et al (1994) revealed a mean level of 25 (OH)D of only 43 nmol/litre with a quarter of the subjects " having frank vitamin D deficiency (<25nmol/l). Not surprisingly the bone mineral density of most of the subjects was very low. Sadly, this study indicates that many people with MS likely do not have enough vitamin D intake to maintain their bones let alone to counter autoimmune reactions. A more recent study by Cosman et al (1998) supported the findings of Nieves et al (1994).

With both the general Paleolithic perspective and the documented low levels of vitamin D in persons with MS in mind, it is worth discussing the role vitamin D plays in the overall development of MS. First of all it is important to differentiate between autoimmunity and autoimmune disease. Autoimmunity is the production of immune cells which are autoaggressive and such a phenonomen has most probably been present throughout human development. It is well established that autoaggressive immune cells are produced during infections (Matzinger, 1998) and the reason for this is that the body must maintain a vast repertoire of immune cells to ensure protection against a huge number of pathogens. Thus the common occurrence of cross-reactive immune cells which react against both foreign and self-antigens represents an evolved compromise between maximum protection against foreign invaders and maximum protection against autoimmunity. Through the actions of the suppressor side of the immune system, evolution has also ensured that the sporadic production of autoaggressive immune cells due to random infections would not go unchecked and result in uncontrolled autoimmunity. Such runaway autoimmunity is called autoimmune disease. Thus, although autoimmunity has always been with us, autoimmune disease is likely a relatively new phenonomen in human development and is due to a relatively recent loss of control (suppression) of sporadically produced autoaggresive immune cells by a portion of the population.

The best explanation for the recent rise in autoimmune disease is that new environmental agents have upset the delicate balance between the production and suppression of autoaggressive immune cells either by increasing autoimmune reactions or by hindering the control of such reactions. When the balance tips towards increased autoimmune reactions and/or decreased suppression, autoimmunity can progress to autoimmune disease. The profoundly different dietary regimen, which began with the adoption of agriculture, is one obvious source of such new, immune-disruptive agents. The Paleolithic diet was dominated by fruits, vegetables and lean wild meats which had a low saturated fat content. The main foods "recently" introduced by agriculture are grains (i.e. grass seed), dairy products and meat from domesticated animals which has a very high saturated fat content. As discussed in detail by Cordain (1999) and Cordain et al (in press), it would appear that proteins from various foods introduced by the Neolithic agricultural revolution (e.g. gluten, dairy, legumes) result in autoimmune reactions mainly by increasing intestinal permeability and by mimicking infectious and self-antigens. The great increase in the consumption of saturated fat also contributes to an increase in inflammatory reactions (Fraser et al, 1999).

Such food-driven autoimmune reactions, although of relatively low magnitude in comparison with infection-driven autoimmune reactions, occur almost on a daily basis. They have a significant cumulative effect and thus recently introduced foods are clearly suitable candidates for the agents which result in harmless autoimmunity becoming problematic autoimmune disease in genetically susceptible persons.

This increase in Neolithic dietary elements that contribute to autoimmune reactions is matched by a notable decrease during the Neolithic of nutrients that play a significant role in the suppression of autoimmune reactions. These suppression-inducing nutrients include both omega 3 fats (fish oil) (Calder, 1998) and vitamin D (references herein). Thus the newly adopted dietary habits of agriculture promote autoimmune disease both by increasing autoimmune reactions and by lessening anti-inflammatory responses. Not surprisingly, MS and other autoimmune diseases are

most common in areas where the dietary regimen contains a dominance of pro-inflammatory food types and a paucity of anti-inflammatory nutrients. The common deficiency of vitamin D is just one of numerous Neolithic nutritional factors which, in combination with the ever present infectious agents, result in a variety of autoimmune diseases in these areas. Consequently, it is just one of a number of factors which must be reversed if one hopes to successfully combat an autoimmune disease.

As discussed above, it appears the best method of reversing vitamin D deficiency is to use a supplement of 4000 IU which will result in optimal levels of vitamin D metabolites. This in turn should result in increased suppression of autoimmune reactions precipitated by food and infectious agents and help to turn the tide against uncontrolled autoimmunity. It seems only reasonable that a person's best hope of controlling an autoimmune disease is to reverse as many of the adverse Neolithic influences, including vitamin D deficiency, as possible.

SUMMARY

An abundance of scientific evidence indicates that vitamin D deficiency is associated with MS onset and progression. Such evidence includes epidemiology which demonstrates that high prevalence rates of MS closely track areas of low intake of vitamin D. Animal experiments reveal that vitamin D hormone can suppress a variety of animal autoimmune diseases including EAE, the animal equivalent of MS. Furthermore, associated immunological studies have shown that vitamin D hormone has a number of immunomodulating functions, all of which contribute to the suppression of inflammatory autoimmune reactions. Small clinical trials have suggested that vitamin D has some efficacy in slowing autoimmune disease progression although no properly controlled trials have been conducted.

Vitamin D can be readily attained from exposure to sunlight and studies have shown that the optimal intake of vitamin D is about 4000- 6000 IU a day. This results in a circulation concentration of 25(OH)D (a vitamin D metabolite) of 100-125 nmol/litre and this level seems to be required for the proper functioning of all vitamin D-dependent systems. In colder, low sunlight areas such an intake from the sun is impossible for most of the year and it is important to use supplements to makeup the shortfall in vitamin D supply. Currently suggested supplement levels of 200-400 IU are much too low. A daily supplement of 4000 IU of vitamin D3 seems warranted for people who do not get a lot of exposure to sunlight throughout the year. This amount is well below the no observed adverse effect level which is conservatively placed at 10000 IU/day and thus such supplementation is safe for anyone who is not hypersensitive to vitamin D.

Throughout most of the two million years of human development, humans had a relatively high intake of vitamin D (~5000-10,000 IU/day) from the sun. Major environmental changes brought on by the agricultural, industrial and technological revolutions have resulted in large populations in northern climates experiencing a subclinical and chronic vitamin D deficiency and this deficiency is more pronounced in persons with MS. Vitamin D deficiency is just one of a number of nutrient-related factors which play a role in MS. Notably the dietary regimens which contain the most pro-inflammatory food types (e.g. gluten, dairy, saturated fat) and the least anti-inflammatory nutrients (vitamin D, omega 3 fats) occur in areas in which MS and other autoimmune diseases are most common. To combat MS, a person must change their lifestyle with diet revision being perhaps the most useful modification. As part of this change, it is important to ensure that sufficient vitamin D (4000 IU/day) is acquired through sun exposure and supplements.

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Sunlight helps beat cancers

Adam Cresswell
Health editor

SUNLIGHT may have beneficial effects on some types of cancer — paradoxically including a type of skin cancer it is known to cause, scientists revealed yesterday.

Their findings, published in the latest issue of the US *Journal of the National Cancer Institute*, show patients with melanoma — one of the deadliest forms of skin cancer — were more likely to survive the disease if they had experienced higher levels of sun exposure.

Another study, also published in the the journal yesterday, confirmed the surprise findings of Australian research published in December that showed sunlight could reduce the risk of developing another form of cancer, non-Hodgkin's lymphoma.

It had been thought that increased sun exposure might be partially to blame for the rising rates of non-Hodgkin's lymphoma worldwide.

But Australian experts who helped conduct the studies warned yesterday that the results were not a licence for people to throw away their sunscreen.

"If Australians want to know whether these findings mean they should ease off on their slip, slop, slapping, the answer is a firm no," said Bruce Armstrong, co-author of the melanoma study and the Australian study on non-Hodgkin's lymphoma.

"We have known for a long time that sun exposure does cause melanoma and other skin cancers, and so Australians must continue to protect their skin," he said.

Professor Armstrong, head of the school of public health at the University of Sydney, said vitamin D, made when the skin is exposed to sunlight, could be the protecting factor.

Just 10 to 15 minutes a day in sunlight before 10am or after 3pm in summer, four to five days a week, was all that was required to benefit, with a few minutes longer in Tasmania.

In winter, just 20 minutes at midday would be required, and slightly less in Brisbane, Darwin and other sunny northern regions of the country.

In the study published yesterday, researchers from the University of Sydney found melanoma patients who had experienced higher levels of sunburn, sun exposure and sun-related damage to the fibrous tissue of the skin were more likely to survive their melanoma.

Andrew Penman, chief executive of the NSW Cancer Council, said the council had provided funds for Professor Armstrong to do a follow-up study.