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The role of vitamin D in multiple sclerosis – observations from Norway

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Abstract

Multiple sclerosis (MS) is a chronic disease of the central nervous system. A relationship between the geographic distribution of MS, exposure to sunlight, and vitamin D metabolism has long been considered. Evidence supporting the UV-radiation/vitamin D hypothesis for MS has been provided by studies of UV-radiation exposure and risk of MS, and by findings indicating that the association of MS with UVR is mediated by vitamin D. In Norway, MS prevalence does not increase with latitude, i.e. decreasing UV-radiation exposure. In coastal areas north of the Arctic Circle, vitamin D sufficiency is maintained by ingested vitamin D from oily fish, cod liver oil and fortified dairy products in addition to exposure of the skin to the sun. However, a possible effect of vitamin D from marine sources cannot be separated from a possible effect of marine n-3 polyunsaturated fatty acids (PUFA). This paper presents observations from Norway supporting a role for vitamin D in the complex aetiology of MS. Possible interactions between sunshine and diet determining vitamin D status are discussed. For a review of the available literature supporting a role of vitamin D in multiple sclerosis the reader is referred to a recent publication (1).

Multiple sclerosis

Multiple sclerosis (MS) is a chronic disease of the central nervous system, affecting young adults, females twice as often as males. The course is usually relapsing-remitting for about 10 years, followed by a secondary progressive

phase. The pathogenetic mechanisms have not been fully elucidated. Histology shows T helper cell type 1-mediated chronic inflammation, demyelination, and axonal degeneration. MS risk is determined by genetic and environmental factors. The window of exposure to environmental factors covers a period of many years, possibly starting in utero. Canadian studies have shown that environmental factors act at a broad population level, not in the familial microenvironment (2).

The UV-radiation/vitamin D hypothesis for MS

A relationship between the geographic distribution of multiple MS, exposure to sunlight, and vitamin D metabolism has long been considered. Formerly, increasing MS rates with distance from the equator were found in the northern and in the southern hemisphere. Evidence supporting the UVR/vitamin D hypothesis for MS has been provided by studies of UV-radiation exposure and risk of MS. MS prevalence in Australia and in France could be closely predicted by regional UVR levels (3, 4). In Tasmania, higher sun exposure when aged 6-15 years was associated with a decreased risk of MS (5). These findings were confirmed in Norway north of the Arctic Circle, where summer outdoor activities in childhood and adolescence decreased MS-risk (6).
More indirectly, mortality from MS was negatively associated with residential and occupational exposure to sunlight (7), and MS was associated with a lower risk of skin cancer, indicating lower exposure to solar radiation in individuals with MS (8). The maternal parent of origin effect and the unexplained excess of MS in those born in May in northern Europe and Canada, might be related to maternal vitamin D insufficiency in winter (9).

There is evidence to support that the association of MS with UVR is mediated by vitamin D. Higher circulating levels of 25(OH) vitamin D were associated with a lower risk of MS in whites (10). Animal studies of the experimental allergic encephalomyelitis (EAE) model for MS have shown that vitamin D hormone completely inhibited EAE induction and progression (11). A role for vitamin D has also been proposed in other immune-mediated diseases: diabetes type I, rheumatoid arthritis, and inflammatory bowel disease (12).

Norway – an exception to the latitude gradient

MS prevalence does not increase with latitude in Norway. Interestingly, the exception of Norway to the latitude gradient for MS parallels the exception of Scandinavia to the latitude gradient that is observed for certain cancers (13). Early epidemiological studies reported a lower incidence of MS in the coastal fishing areas than in the inland farming and dairy areas (14). When Lauer

reviewed the available evidence in 1997, he concluded that an increased MS risk associated with consumption of animal fat, animal protein and meat was more likely than a protective effect of fish intake (15).

Assuming that the association of MS with latitude is mediated by vitamin D, vitamin D status and sources of vitamin D in Scandinavia deserve more attention. Subclinical vitamin D deficiency wintertime is surprisingly more common in southern Europe than in Scandinavia (16, 17). Even north of the Arctic Circle, sun exposure contributes significantly to serum 25(OH) vitamin D levels, and summer outdoor activities in childhood and adolescence decreased MS-risk (6). High dietary intake of vitamin D, especially in winter, largely compensates for the effect of seasonal variation in UVR-exposure north of the Arctic Circle (18). Fatty seafood, egg yolks, and chanterelle mushrooms are the only foods that naturally contain a considerable amount of vitamin D. In Norway at latitudes 65-71°N, the main sources of ingested vitamin D are salmon and trout (30%), cod-liver oil supplements (23%), and fortified margarine or butter on bread (23%) (17). In North Norway, consumption of fish three or more times a week was associated with reduced risk of MS, and supplemental cod-liver oil was possibly protective against MS when sun exposure was less (6). The UVR/vitamin D hypothesis is strengthened by these findings, suggesting a protective role of ingested vitamin D.

A more comprehensive paper summarising observations from Norway supporting the UVR/vitamin D hypothesis for MS and discussing a possible role of PUFA has been published recently (19).

A role for marine n-3 polyunsatured fatty acids in MS risk?

Both fatty fish and cod-liver oil contain considerable amounts of marine n-3 polyunsaturated fatty acids (PUFA) as well as vitamin D. The per capita intake of n-3 PUFA in Norway is approximately four times as high as in the U.S. (20). Both vitamin D and PUFA have immunosuppressive properties and are involved in brain development and differentiation, neuroprotection and regeneration, all mechanisms that are relevant in MS pathogenesis.

Conclusion

The UVR/vitamin D hypothesis is strengthened by findings suggesting a protective role of ingested vitamin D north of the Arctic Circle where UVR exposure is low. However, the effect of vitamin D from dietary sources cannot be separated from a possible effect of marine n-3 PUFA.

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