Could vitamin D be the answer to multiple sclerosis?

Clinical and pathological studies would suggest that multiple sclerosis is a heterogeneous disease with individual patients varying dramatically in the extent of inflammatory change and axonal loss [1]. Relapses and inflammation appear to be due to an immune system in overdrive with the oligodendrocyte as a possible primary target of what most are agreed is an autoimmune process [2]. Whilst axonal loss was once thought to be a secondary phenomenon, the rediscovery of early axonal loss in at least some cases of multiple sclerosis has raised new questions regarding this apparently degenerative component of the disease [1]. The importance of this is emphasized in the lack of responsiveness to immunomodulatory therapies and even immune ablating therapies with an inexorable decline continuing in up to one third of patients [3].

What is the genesis of this dysregulated immune attack in multiple sclerosis? Considerable steps forward in answering this question have come from epidemiological studies over the last 100 years. The importance of genetics has been clearly demonstrated [4]. However, despite intensive worldwide efforts the only locus to have confirmed linkage and association in multiple sclerosis is HLA-DR in the major histocompatibility complex on chromosome 6 [5]. The current conclusion is that any further genes conferring susceptibility to multiple sclerosis will be of very small effect and possibly beyond the threshold of detection with currently available technologies and sample sizes.

What else has epidemiology taught us regarding the possible causes of multiple sclerosis? Studies of migrant populations are always difficult but most studies tend to suggest confinement of a risk approaching that of the local destination population particularly if migration occurs before the age of 15 [6]. The worldwide geographical distribution of multiple sclerosis – common in populations of Northern European origin and rare in almost all others can be explained on the basis of genetic differences [7]. However, studies of relatively genetically homogenous populations show a variation in prevalence with latitude [8]. These two lines of evidence point towards some environmental factor as being important.

Environmental factors which have effectively been excluded as risk factors for multiple sclerosis include trauma [9], dental amalgam [10] and occupational exposure [11]. Factors which have good evidence for a role are smoking [12] and Epstein-Barr virus [13] but neither of these would seem to explain the latitudinal gradient.

Recent long term cohort studies have suggested a role for vitamin D deficiency in susceptibility to multiple sclerosis [14]. Animal studies have shown that vitamin D deficiency has an effect on the immune system [15] and on the brain [16]. The existence of a four-way correlation between multiple sclerosis prevalence, latitude, sun exposure and vitamin D levels [17] does not distinguish which component may be causative or if there is some other confounder which has yet to be identified. However, a detailed study of historical reporting of sun-exposure, objective measures of sun damage to skin and risk of multiple sclerosis within a relatively restricted latitudinal band (Tasmania) has suggested that this may be more than a coincidental correlation and that absolute or relative vitamin D deficiency may indeed be causal [18].

The study design reported by Lucas et al. [19] in this edition of multiple sclerosis outlines the proposed Ausimmune Study. Through careful study of incident cases at four different latitudes and using tried and tested methods we should be optimistic that this study will clarify the issue of causality in the relationship between, latitude, sun-exposure, vitamin D levels and multiple sclerosis risk.

There have already been calls for routine use of vitamin D supplementation [20]. However, given the potential for harm from vitamin D toxicity and the lack of evidence with regards to the efficacy of oral vitamin D supplementation the correct approach is to await the outcome of the Ausimmune study. Furthermore, given the experience from the genetic analysis of multiple sclerosis it seems likely that the environmental epidemiology will also turn out to be complex and heterogeneous. We should therefore await the results of appropriate scientific research before embarking on wholesale prevention or treatment programmes. The answer to the question posed in the title of this editorial is, ‘possibly, but let’s wait for the evidence’.
References


