The increasing incidence and prevalence of female multiple sclerosis--a critical analysis of potential environmental factors.

Multiple sclerosis (MS) is the most common acquired inflammatory demyelinating disorder of the central nervous system (CNS). Not unlike many inflammatory diseases with a presumed autoimmune pathogenesis, it has been established that there is a female preponderance in prevalence. While in the past it was shown that there are two women for every man with a diagnosis of MS, recent serial cross-sectional assessments provide compelling evidence for an increase of the female to male sex ratio in patients with relapsing-remitting MS over the last decades. An understanding of this phenomenon might provide key insights into the pathogenesis of the disease but also may have implications for health-care strategies and further research efforts. We review possible etiologies for the gender disparity in MS, and we discuss possible underlying causes. We determined that the biologically most plausible explanations for a disproportional increase of MS among women in some population may be the role of vitamin D in MS pathogenesis. Decreased sun exposure may be a critical factor in diminished vitamin D levels in many recent cohort studies. Vitamin D insufficiency or deficiency has been shown to affect T cell differentiation and regulation, which may affect cellular immune responses against autoantigens and pathogens that have been associated with the etiology of MS. Vitamin D also appears to impact B cell activation and
differentiation, another cell type that has been implicated in the inflammatory cascade underlying CNS autoimmune disease.