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MULTIPLE SCLEROSIS

# Vitamin D deficiency leads to excessive B-cell responses in multiple sclerosis

Vitamin D deficiency upregulates the immunoreactivity of B cells in patients with multiple sclerosis (MS), according to a new study. The finding supports the hypothesis that vitamin D supplementation could have a disease-modifying role in the management of MS.

Many studies have established that low levels of vitamin D are a risk factor for MS, but the exact nature of the effect is unclear. "Available data suggest that vitamin D in sufficient concentrations downregulates the activity of immune cells, in particular T lymphocytes," explains Jürgen Haas, lead author of the new study. "The role of B cells in MS has been emphasized by the therapeutic efficiency of B-cell-depleting antibodies, but data on the interaction of vitamin D and B cells is scarce."

Haas and colleagues studied this interaction in 95 patients with relapsing–remitting MS, almost half of whom had hypovitaminosis D — a serum level of the metabolite 25-hydroxyvitamin D (25(OH)D) below 20 ng/ml. They combined measurements of 25(OH)D in the blood and cerebrospinal fluid (CSF) of patients with *in vitro* cell-based experiments to assess the effects of vitamin D on B cell immunoreactivity.

B cells isolated from 28 patients with MS exhibited greater proliferation and release of IL-6 in response to immunostimulants than did B cells from healthy controls or individuals with other disorders, and immunoreactivity was particularly high in the cells from MS patients with hypovitaminosis D. Incubation of isolated B cells in different concentrations of the active metabolite of vitamin D demonstrated that the immunoreactivity of these cells was dependent on the dose of the metabolite.

MS patients with hypovitaminosis D had higher Expanded Disability Status Scale scores and more-frequent relapses than did MS patients with sufficient vitamin D, indicating more-severe disease. In 12 patients whose B-cell function was assessed before and after taking vitamin D supplements, the B-cell proliferative response and IL-6 release was decreased after supplementation.

Haas and co-workers also showed that hypovitaminosis D translates into CNS effects. "Patients with a low vitamin D status exhibited decreased vitamin D levels in the CSF and more-marked intrathecal enrichment of antigen-experienced, class-switched memory B cells and antibody-secreting plasma cells," says Haas. "These data support the hypothesis that hypovitaminosis D in the blood and CSF act together to negatively interfere with immune responses outside and inside the CNS."

The researchers conclude that the effects of vitamin D deficiency on B cells exacerbate disease activity in MS, indicating that ongoing trials of vitamin D supplementation are likely to demonstrate therapeutic effects.

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> "the effects of vitamin D deficiency on B cells exacerbate disease activity in MS"

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