Environmental risk factors for the occurrence of multiple sclerosis

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt förvar i Hörsal B, Målpunkt T, vån 9, NUS, fredagen den 17:e april, kl. 09:00.
Avhandlingen kommer att försvaras på svenska.

Fakultetsopponent: Professor, Kjell-Morten Myhr, Nevrologisk avdelning, Haukeland universitetssjukehus, Universitet i Bergen, Norge.

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Abstract

Background. Multiple sclerosis (MS) is an inflammatory and degenerative disease of the central nervous system that typically debuts around age 30. About 2.3 million people are affected in the world today, and besides trauma it is the most common cause of neurological disability among young adults in the western world. The disease likely develops via a complex interplay of genetic vulnerability and environmental risk factors, and adolescence is assumed to be a critical time for disease initiation. The aim of this study was to investigate how MS risk in different age groups is influenced by vitamin D, infections with Epstein-Barr virus and Human herpesviruses 6A and B as well as the metabolic markers leptin and insulin.

Methods. In this nested case-control study we identified pre-symptomatically drawn blood samples from individuals below age 40, that later developed relapsing remitting MS. This was done through crosslinking of the Swedish MS registry, or a local database, with six Swedish biobanks containing remainders of samples used in microbiological analyses. For each case, one control matched for biobank, sex, date of sampling and age of sampling was selected. These samples were then analysed to determine antibody reactivity against Epstein-Barr virus and Human herpesvirus 6A and B, as well as measure concentrations of leptin, insulin and 25-hydroxyvitamin D. The effect of these variables on MS risk was estimated using conditional logistic regression, both in the entire case-control material as well as stratified into three groups by age at sampling (<20, 20-29 and 30-39) and by sex.

Results. Human herpesvirus 6A, but not B, was consistently associated with an increased risk of developing MS. In contrast, Epstein-Barr virus demonstrated an age dependent pattern indicating that early infection may be protective against MS while later infection increases the risk. As for the metabolic markers, insulin was not associated with MS while elevated levels of leptin showed an association with increased MS risk both among individuals below 20 years of age and among all men. For women there was instead an inverse association in the oldest group, aged 30-39, when adjusting the leptin analysis for insulin concentrations. Finally, having vitamin D concentrations in the top quintile was associated with decreased MS risk, without evidence of a stronger effect in young subjects.

Conclusion. These results implicate Human herpesvirus 6A and leptin as risk factors for MS development. They also further support a protective role for vitamin D in MS etiology and provide serological evidence of an age dependency of Epstein-Barr virus infection as it relates to MS risk.

Keywords
Multiple sclerosis, risk factors, epidemiology, case-control study, Human herpesvirus 6A, Human herpesvirus 6B, leptin, insulin, Epstein-Barr virus, vitamin D