

# Risk factors multiple sclerosis

## Lifestyle and Environment in MS

**Table 1.** Summary of established and tentative lifestyle/environmental factors and their potential interaction with multiple sclerosis (MS) human leukocyte antigen (HLA) risk genes

| Factor                         | OR   | HLA gene interaction | Combined OR | Effect mainly during adolescence | Immune system implied |
|--------------------------------|------|----------------------|-------------|----------------------------------|-----------------------|
| Smoking                        | ~1.6 | +                    | 14          | No                               | +                     |
| EBV serology                   | ~3.6 | +                    | ~15         | Yes                              | +                     |
| Vitamin D <50 nM               | ~1.4 | No                   | -           | Probably                         | +                     |
| Adolescent obesity/<br>BMI >27 | ~2   | +                    | ~15         | Yes                              | +                     |
| Night work                     | ~1.7 | No                   | -           | Yes                              | +                     |
| Low sun exposure               | ~2   | No                   | -           | Probably                         | +                     |
| Infectious<br>mononucleosis    | ~2   | +                    | 7           | Yes                              | +                     |
| Passive smoking                | ~1.3 | +                    | 6           | No                               | +                     |
| Oral tobacco/nicotine          | 0.5  | nd                   | -           | Unknown                          | +                     |
| Alcohol                        | ~0.6 | nd                   | -           | Unknown                          | +                     |
| Coffee                         | ~0.7 | nd                   | -           | Unknown                          | +                     |

OR, Odds ratio; EBV, Epstein-Barr virus; BMI, body mass index; nd, not determined.

There is a clear dose–response relationship,  
in which the cumulative dose of smoking is related to a risk  
increase

Cotinine levels in sera/plasma ( $\geq 10$  ng/mL),

**Second-hand** exposure to smoke has also been associated with increased risk for MS, which suggests that even **minor “lung-irritation”** may be important .If the association is because of nonspecific irritation, one might even consider a factor such **as air pollution**

smoking also increases  
the risk of developing **neutralizing antibodies**  
**against** biologics used in treatment of MS, including  
**natalizumab** (Hedstrom et al. 2013a) and **interferon $\beta$**

To distinguish between roles of nicotine from other tobacco constituents that are inhaled in the lung, the **Swedish population** is suitable because the use of **oral tobacco** in the form of moist snuff is very common. **Oral tobacco (snuff) shows a dose-dependent association with a lessened risk of MS** (Hedstrom et al. 2009, 2013c). Nicotine is the primary candidate for such possible protection in view of its action on the  **$\alpha 7$  subunit of the acetylcholine receptor present on immune cells,**