

Managing Disease Progression: Is Lifestyle Modification Worth It?

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Disclosures

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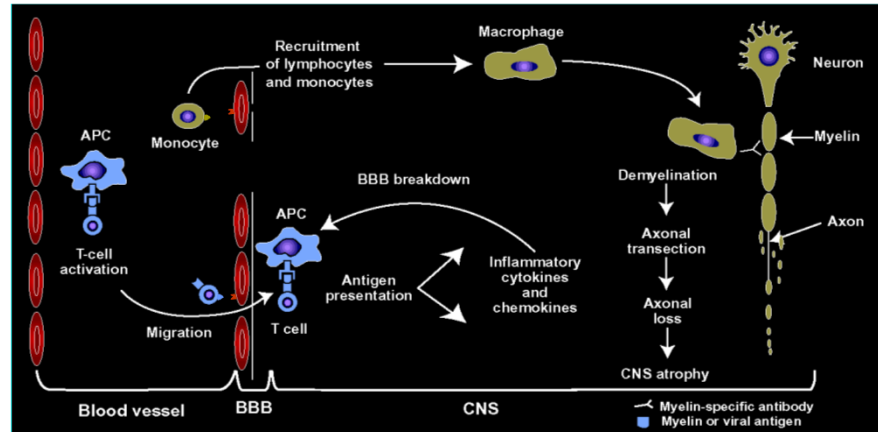
Learning Objectives

- To learn about effects of lifestyle on clinical MS disease progression
- To learn about links between lifestyle and factors that impact MS disease activity

Lifestyle Modifications

- Dietary factors
- Exercise
- Sleep
- Stress
- Smoking

MS is an Immune-Mediated Disease



BBB=blood-brain barrier; APC=antigen-presenting cell.
Adapted from Miller et al. *Continuum: Multiple Sclerosis (Part A)*, 1999;5:7.

Effects of Diet on Immune Function

- Pro-inflammatory:
 - Saturated fats (eggs, cheese, other dairy); trans-fats
 - Omega-6 FA's (corn, safflower, sunflower, grapeseed, soy, peanut, and vegetable oils)
 - Refined carbohydrates (white flour and rice)
 - Gluten, casein
 - Excess alcohol
 - Sodium
- Anti-inflammatory:
 - Omega-3 fatty acids
 - Vitamin D

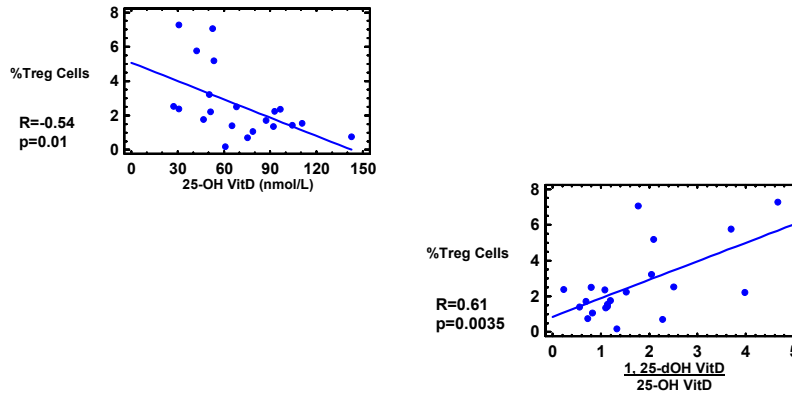
Diet and MS Disease Course

- Diet effects are not conclusive
- Swank et al (1990): less progression and lower death rate with a low fat diet (the disease course was variable in the two groups)
- Lauer (1997): review of multiple studies suggest benefit from low fat and marine (seafood) diet
- Microbiome
 - Protection in EAE from *Bacteroides fragilis* polysaccharide A
 - Obesity is associated with decreased *Bacteroides* species

Vitamin D and MS

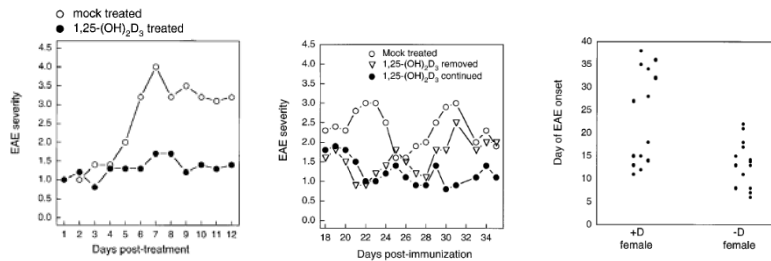
- Epidemiological studies
 - MS incidence is higher in areas of world that are farthest from the equator
 - The disease is less common in coastal areas (abundance of fatty fish, fish oils, vitamin-D rich seafood)
- Immunological studies
 - Vitamin D suppress proinflammatory response and enhances anti-inflammatory responses
- Pre-clinical studies
 - Suppresses experimental MS-like disease in animals
- Clinical studies
 - Effects on microbiome can be observed
 - Clinical efficacy has not been proven to date

Vitamin D Measurements and Regulatory T Cell Percentages



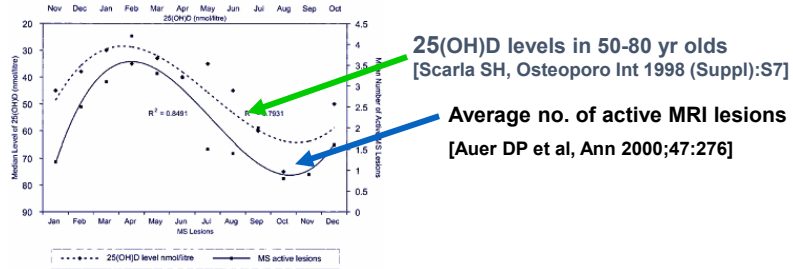
Royal W, et al. J Neuroimmunol 2009; In press.

1, 25-dOH VitD Reversibly Blocks Relapsing EAE



Cantorna MT et al. PNAS 1996;93:7861.

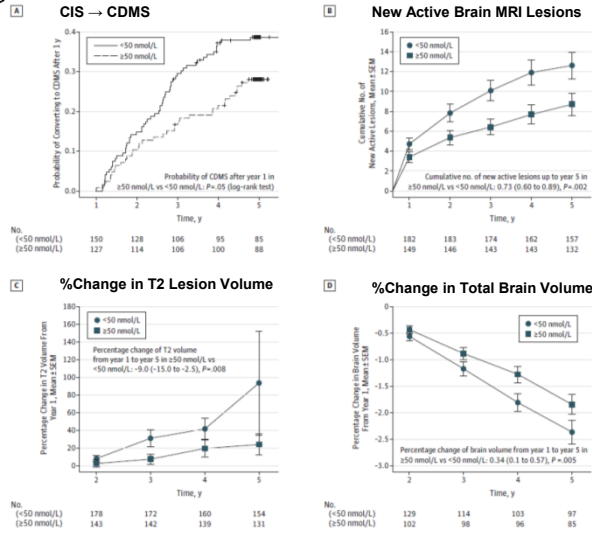
Variation in MRI and Serum Vitamin D Levels



Normal and Deficient 25-hydroxyl Vitamin D Blood Levels

<u>Measurement</u>	<u>Range</u>
Normal range	75-185 nmol/L (30.0-74.0 ng/mL)
Vitamin D insufficiency	50-75 nmol/L (20-30 ng/ml)
Vitamin D deficiency	<50nmol/L (20 ng/ml)

Effect of Vitamin D Deficiency (<50 nmol/L) on MS Clinical Outcomes



Ascherio et al, JAMA Neurology, 2014.

Evidence for Beneficial Effects from Vitamin D Supplementation

- Decreased conversion from CIS
- Improved immunological parameters
- Benefit from administration of vitamin D analogue

Cigarette Smoking and MS

- Smoking is associated with
 - An increased risk of MS
 - More rapid MS disease progression
 - Greater likelihood of MS treatment failure
 - Development of anti-IFN β and anti-natalizumab antibodies
 - Increased risk of MS among children of cigarette smokers
 - Conversion of relapsing-remitting to progressive disease

Components in Cigarette Smoke

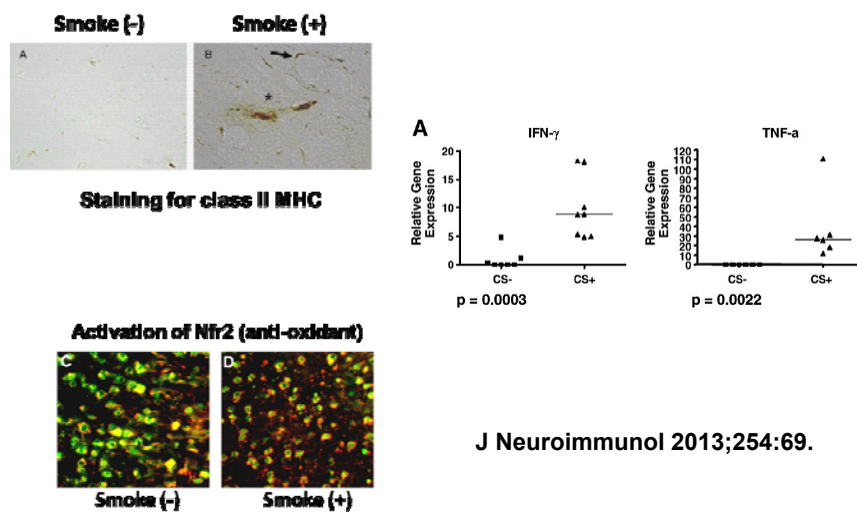
Over 4,000 chemical components, including:



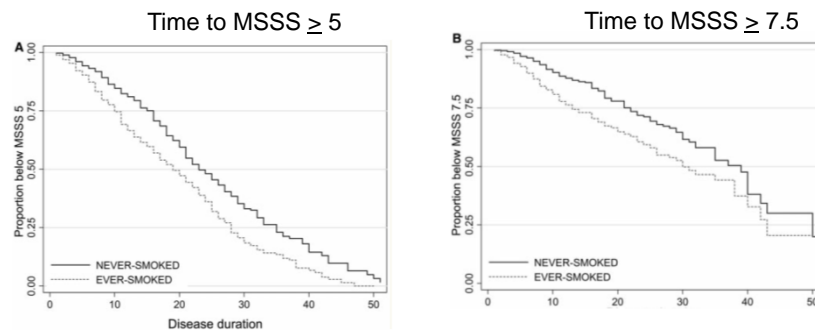
Immune Effects of Smoking

- Increased circulating markers of inflammation
 - 30% increase in peripheral white blood cell counts
 - Increased CD4+ and CD8+ T cell numbers
 - Individuals with >50 pack year history of smoking (heavy smokers) have depressed CD4+ and increased CD8+ T cell numbers
 - With cessation, improvement in numbers may be delayed for as long as 2-4 years

Cigarette Smoking and Brain Inflammation



Tobacco Smoking and Disability Progression



Manouchehrinia, A et al. Brain 2013; 136:2298.

Treatment: Cessation

- Individual counseling
- Nicotine replacement therapy
 - Approved products: gum, skin patches, lozenges, oral inhaled products, and nasal spray
 - Electronic cigarettes: Not currently FDA-approved
- Medications
 - Varenicline (Chantix)
 - Bupropion (Wellbutrin)
- Smoking cessation programs

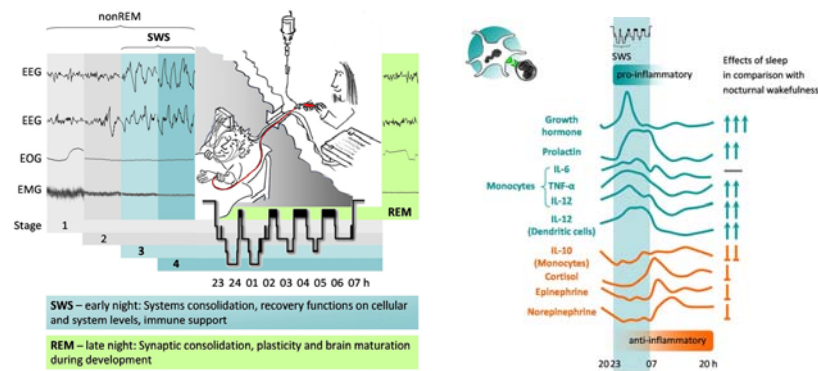
Stress and MS

- Chicken or egg?
 - MS can affect mood, increase risk of depression, induce stress
 - Inflammatory cytokines (TNF- α , IL-6, IL-1 β , IFN- γ) can increase depressive symptoms (Puchak M, 2007)
 - Depression decreases production of brain-derived neurotrophic factor (BDNF)
 - Stress induces dysfunction of the hypothalamic pituitary axis and autonomic nervous system

Sleep and MS

- Sleep disorders are common in MS
- Cytokines act as regulators and inducers of phases of sleep
- White blood cells show circadian patterns and increase in number and activity with sleep deprivation

Sleep Physiology and Immunity



<http://brainimmune.com/t-cell-and-antigen-presenting-cell-activity-during-sleep/>

Exercise and MS

- Combats obesity and its negative effects
- Improves stamina, lessens fatigue
- Improves muscle tone and function
 - Beneficial effects on musculature of bladder and GI tract
- Stimulates secretion of neurotrophic factors (BDNF)
- Strengthens bones, joints
- Beneficial effects on mood and secondary consequences

Conclusions

- Issues of lifestyle can impact not only the risk of MS but also rates of MS disease progression
- Such effects can also potentially modify responses to MS therapies