Best-Bet Diet / Supplements/Lifestyle for MS – Dr Angus Nisbet Aug 2018

There is no clear evidence that any of these measures affects relapse frequency or progression of disability in MS and hence the term 'best-bet'

- **Vitamin D3** at least 3000units
  - Low vitamin D levels have been associate with the development of MS in multiple studies
  - There is conflicting evidence whether supplementation with vitamin D in patients with MS, reduces relapse rate.

- **Omega 3,6 and 9 supplements Polyunsaturated fatty acids (PUFAs)** eg fish oil, Evening Primrose, oil and either sunflower, olive, avocardo or nut oil.
  - Omega 3,6 and 9 are essential fatty acids that the body cannot make and which are used as building blocks for brain and nerve tissue
  - Overall, there is some evidence that they may reduce relapse rate in RRMS

- **Healthy & Balanced Diet**
  - possibly with some antioxidants would seem sensible eg red fruit
  - It would also seem sensible to avoid food that "upsets" you , because this might theoretically trigger immune responses and MS is an auto-immune condition

- **Healthy Lifestyle**
  - Get at least 7 hours sleep
  - If you are tired, then sleep. Take a nap if you feel you need one.
  - Take daily high-intensity, short-duration cardiovascular exercise. An exercise-bike or cross-trainer in the house makes this easier. Remember: *'the only bad work-out is the one you didn't do!'*
  - Don't get run down / over-stressed
  - If you have an infection of any sort, then rest and be kind to yourself

- **Biotin** may improve disability in primary progressive MS according one trial and vision in progressive optic neuritis in another trial. A further bigger trial is expected to finish in September 2019. https://www.mssociety.org.uk/ms-research/treatments-in-the-pipeline/MD1003

- **Simvastatin.** For SPMS, it may also be worth going on a statin, if you can persuade your GP.
  - One UK trial in humans with SPMS showed reduced brain shrinkage with high-dose simvastatin (80mg/day).
  - Here is a meta-analysis of statin therapy in MS: http://www.ncbi.nlm.nih.gov/pubmed/25795002
  - Now an ongoing London-based national trial (MS STAT2) which you may be able to enrol in locally:
  - Inclusion criteria: Secondary progressive MS, aged 25 to 65 years old EDSS 4.0-6.5, not taking a statin within 6 months of trial entry, not on a disease modifying immunological drug. Contact: Raquel Nsue-Sha Akieme, Clinical Research Nurse, CIRU, Royal Sussex County Hospital, Tel: 01273 696955 ext 3907.

- **CBD – Cannabidiol Oil.** This is the non-euphoriant ingredient of cannabis oil. It has theoretical anti-inflammatory, antioxidative, antiemetic, antipsychotic, and neuroprotective. effects. There is limited evidence that it may reduce pain, fatigue, spasticity, and ultimately and may even improve mobility. It can interfere with the metabolism of prescription drugs and is sometimes mixed with tetrahydro-cannabidiol which is euphoriant. There is no long-term safety data https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5874292/

JAMA Neurol. 2018 Aug 1;75(8):1013-1021. doi: 10.1001/jamaneurol.2018.0611.

Use of Vitamins and Dietary Supplements by Patients With Multiple Sclerosis: A Review.

Evans E[1], Piccio L[1], Cross AH[1].

Table 1. Summary of Evidence for Vitamin Use in Multiple Sclerosis (MS)

Vitamin	Category	Recommended Daily Allowance	Tolerable Upper Intake Level	Evidence in Animal Models	Effects Noted in MS	Serious Toxic Effects	Level of Evidence[a]	Key References
A (carotenes, retinol)	Antioxidant, anti-inflammatory	Men, 2970 IU; women, 2310 IU	10 000 IU	↓ EAE severity with treatment	Treatment ↓ IL-17, RORγt, T-bet, and IFN-γ, ↑ TGF-β and FoxP3, improved fatigue	Psychiatric, liver failure, cerebral edema	2	4-6
B_1 (thiamine)	Antioxidant	Men, 1.2 mg; women, 1.1 mg	Unknown	Low levels ↑ CCL-2, activated microglia, promoted T-cell infiltration, and T_H1 and T_H17 cells	Treatment improved fatigue	None	5	7,8
B_2 (riboflavin)	Antioxidant	Men, 1.3 mg; women, 1.1 mg	Unknown	Low levels impaired myelination; treatment ↓ motor impairment, ↑ BDNF, IL-6, and IL-17A	None	None	2	9-11
B_3 (niacin)	Antioxidant; anti-inflammatory	Men, 16 mg; women, 14 mg	Not universal (<1000 mg)	Treatment activated HCA2 receptor, ↓ NFκB and chemotactic signals	None	Liver toxic effects	Insufficient evidence	12,13
B_5 (pantothenic acid)	Metabolic agent	5 mg	Unknown	None	None	None	Insufficient evidence	None
B_6 (pyridoxine)	Antioxidant	Men, 1.7 mg; women, 1.5 mg	100 mg	None	None	Sensory neuropathy	Insufficient evidence	14-16
B_7 (biotin)	Metabolic agent	30 μg	Unknown	None	Treatment resulted in clinical improvement, including visual acuity, muscle strength, VEPs, fatigue, coordination, and mood symptoms	None	1	17,18
B_9 (folic acid)	Metabolic agent	0.4 mg	1 mg	None	None	None	Insufficient evidence	19
B_{12} (cobalamin)	Metabolic agent	2.4 μg	Unknown	Low levels ↓ myelin integrity; treatment ↓ motor deficits in combination with IFN-β (compared with animals given IFN-β alone)	Negatively correlated with VEPs	None	5	19-22
C (ascorbic acid)	Antioxidant	Men, 90 mg; women, 75 mg	2000 mg	None	None	Kidney stones	Insufficient evidence	23,24
D (D_3: cholecalciferol; D_2: ergocalciferol)	Multiple functions	600-800 IU	4000 IU	Treatment modulated T cells, B cells, and dendritic cells, ↓ IL-22, ↑ CCL-2, ↓ EAE severity	Treatment ↓ rate of relapse and of lesions found by MRI	Hypercalcemia, arrhythmias, kidney stones	1	25-28
E (tocopherols and tocotrienols)	Antioxidant	22.4 IU	1000 IU	Treatment ↓ EAE severity, delayed onset of EAE	None	Excessive bleeding risk	Insufficient evidence	29,30

Abbreviations: ↓, decreased; ↑, increased; BDNF, brain-derived neurotrophic factor; CCL-2, chemokine (C-C motif) ligand; EAE, experimental autoimmune encephalomyelitis; FoxP3, forkhead box P3; HCA2, hydroxycarboxylic acid receptor 2; IFN, interferon; IL, interleukin; MRI, magnetic resonance imaging; NFκB, nuclear factor κB; RDA, recommended daily allowance; RORγt, retinoic acid-related orphan receptor γt; TGF, transforming growth factor; T_H, helper T cell; UL, tolerable upper intake level; VEPs, visual evoked potentials.

[a] Levels of evidence based on the Quality Rating Scheme for Studies and Other Evidence modified from the Oxford Centre for Evidence-based Medicine for rating of individual studies; available online at https://www.cebm.net/2016/05/ocebm-levels-of-evidence/.

Table 2. Summary of Evidence for Other Dietary Supplement Use in Multiple Sclerosis (MS)

Supplement	Category	Tolerable Upper Intake Level	Evidence in Animal Models	Effects Noted in MS	Toxic Effects	Level of Evidence[a]	Key References
Caffeine	Stimulant, metabolic agent	1200 mg	Treatment up-regulated adenosine 1 A; enhanced the blood-brain barrier	Treatment showed potential reduction in risk of MS	Arrhythmias, seizures	3	31-34
Carnitine (acetyl-L-carnitine)	Metabolic agent	Unknown	None	Treatment showed potential reduction of fatigue	Medication interactions	2	35,36
Coenzyme Q10 (ubiquinone)	Antioxidant	Unknown	Treatment improved EAE, ↓ TNF, IL-6, IL-17, axonal degeneration, NFκB cascade, and mitochondrial complex 1	Treatment ↓ TNF, IL-6, and MMP and showed potential reduction of fatigue and depression	Hepatotoxic effects	3	37-39
Creatine	Antioxidant, cytoprotective	Unknown	Treatment was protective of oligodendroglial cell loss	None	Renal failure	Insufficient evidence	40
Curcumin	Antioxidant, anti-inflammatory	Unknown	Treatment improved EAE, ↓ T_H17 and chemotactic cytokines	None	Potential hepatoxic effects	Insufficient evidence	41
Gingko biloba	Antioxidant	Unknown	None	Potential improvement in mood, cognition, and fatigue	Medication interactions	3	42,43
Green tea extract (EGCG)	Antioxidant, anti-Inflammatory	Unknown	Treatment ↓ IFN-γ, 1L-17, IL-6, IL-1b, TNF, T_H1 and T_H17 cells, and motor dysfunction	None	Acute liver failure	4	44,45
Lipoic acid	Antioxidant	Unknown	Treatment ↓ EAE severity and lymphocyte migration into CNS	↓ MMP-9, ICAM-1, IFN-γ, and whole-brain atrophy in SPMS	Medication interactions, hypoglycemia, kidney toxic effects	1	46,47
Polyunsaturated fatty acids	Antioxidant	Unknown	Treatment ↓ IFN-γ, IL-17, and MMP, modulated T cells	Potential decrease in no. of relapses, potential reduction in fatigue	Increased bleeding risk, hypoglycemia	2	48
Probiotics	Other	Unknown	Treatment reduced EAE, modulated T cells	Potential improvement in clinical markers and mood	None	2	49-51
Resveratrol	Antioxidant, anti-inflammatory	Unknown	Treatment had mixed results, improved optic neuritis, ↓ motor signs of EAE, strengthened blood-brain barrier, ↓ NFκB, worsened EAE, ↑ IL-17	None	Increased bleeding risk, medication interactions	Insufficient evidence	52-54

Abbreviations: ↓, decreased; ↑, increased; CNS, central nervous system; EAE, experimental autoimmune encephalomyelitis; EGCG, epigallocatechin-3-gallate; ICAM, intercellular adhesion molecule; IFN, interferon; IL, interleukin; MMP, matrix metallopeptidase; NFkB, nuclear factor κB; SPMS, secondary progressive MS; T_H, helper T cell; TNF, tumor necrosis factor.

[a] Levels of evidence based on the Quality Rating Scheme for Studies and Other Evidence modified from the Oxford Centre for Evidence-based Medicine for rating of individual studies; available online at https://www.cebm.net/2016/05/ocebm-levels-of-evidence/.