

Multiple Sclerosis

Overview

Multiple sclerosis is a chronic, autoimmune disease of the central nervous system characterized by increased inflammation and degradation of the myelin sheath on neural axons.¹ The disease begins with a breakdown of the blood brain barrier and resultantly, an increased permeability of the brain to leukocytes and other immune cells from the rest of the body.² Oligoclonal T lymphocytes and B lymphocytes are two major populations of cells that attack the myelin sheath coverings.³ The damage to the myelin sheath coverings results in a variety of symptoms including but not limited to weakness, muscle tingling, numbness, cognitive decline, and walking difficulties.⁴ There are four diagnosable varieties of multiple sclerosis: relapsing-remitting, secondary progressive, primary progressive, and progressive relapsing⁵. The etiology of all four types of multiple sclerosis remains unknown, but the disease appears more commonly in females⁶ and individuals living at higher latitudes.⁷ The relationship between latitude and multiple sclerosis appears to be related to relative exposure to ultraviolet radiation from the sun.⁷ Current treatments include a variety of medications in combination with physical therapy. Acute relapse management medications include corticosteroids, like methylprednisolone, which reduce the severity and inflammation of relapses.⁸ Disease-modifying drugs, such as interferon-beta,⁹ glatiramer acetate,^{10,11} and natalizumab,¹² effectively reduce relapse rates, inflammation, and slow disease progression. Current medications help improve the patients' overall health and quality of life, but their effects come alongside a wide variety of side effects. Side effects range in severity and vary depending on the medication. Corticosteroids can generate insomnia and increased blood pressure, while disease-modifying therapies can cause injection site inflammation,¹³ liver damage,¹⁴ and, in rare cases, a life-threatening infection of the brain known as progressive multifocal leukoencephalopathy (PML).¹⁵

Diet

A limited amount of research has been conducted on the diet's influence on multiple sclerosis, preliminary research, however, demonstrates that diet may be a valuable point of intervention for individuals suffering from multiple sclerosis, as it has been connected to the etiology¹⁶ and progression^{17,18} of the disease. Generally speaking, the Standard American Diet and the resultant increase in triglyceride¹⁹ and LDL cholesterol levels,²⁰ are associated with a quicker progression of the disease. Contrastingly, the Mediterranean diet and consumption of fruits, vegetables, and fish, decreases the likelihood of developing multiple sclerosis.²¹ In terms of dietary supplements, vitamin D₃ insufficiency^{22,23} and decreased omega-3 fatty acid intake^{22,24} are both well-established risk factors for multiple sclerosis development. Decreased vitamin D₃ consumption in mothers during pregnancy has even been associated with a higher risk of multiple sclerosis development in the fetus.¹⁶ Supplementation of omega-3 fatty acids and vitamin D₃ has also shown effective in slowing the progression of the disease²⁵⁻²⁷ in individuals already diagnosed. Vitamin D₃ and omega-3 fatty acid supplements may be safely taken simultaneously, and research even suggests that the combination of the supplements helps slow multiple sclerosis progression.²⁵ Vitamin D₃ supplements can be taken in the form of fish oil tablets, with 0.5g Docosahexaenoic acid (DHA) and 0.4g eicosapentaenoic acid (EPA),¹⁸ while vitamin D₃ supplements can safely be consumed up to the upper limit of 4,000 IU.²⁸ Additionally, calcium and vitamin D₃ supplements may be helpful for patients taking corticosteroids, which can create an unhealthy reduction the body's absorption of calcium.²⁹

Diet and dietary supplementation are great addition to current therapies but should not be considered a replacement for medications and physical therapy. Many studies have shown that dietary changes in conjunction with interferon beta^{26,27} or glatiramer acetate^{17,26} treatment significantly improve multiple sclerosis patients' disease progression.

References

1. Trapp BD, Peterson J, Ransohoff RM, Rudick R, Mörk S, Bö L. Axonal transection in the lesions of multiple sclerosis. *N Engl J Med*. 1998;338(5):278-285. doi:10.1056/NEJM199801293380502
2. Shinto L, Marracci G, Baldauf-Wagner S, et al. Omega-3 fatty acid supplementation decreases matrix metalloproteinase-9 production in relapsing-remitting multiple sclerosis. *Prostaglandins Leukot Essent Fatty Acids*. 2009;80(2-3):131-136. doi:10.1016/j.plefa.2008.12.001
3. Wucherpfennig KW, Newcombe J, Li H, Keddy C, Cuzner ML, Hafler DA. T cell receptor V alpha-V beta repertoire and cytokine gene expression in active multiple sclerosis lesions. *J Exp Med*. 1992;175(4):993-1002. doi:10.1084/jem.175.4.993
4. MS Symptoms : National Multiple Sclerosis Society. <https://www.nationalmssociety.org/Symptoms-Diagnosis/MS-Symptoms>. Accessed November 11, 2019.
5. Lublin FD, Reingold SC. Defining the clinical course of multiple sclerosis: results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis. *Neurology*. 1996;46(4):907-911. doi:10.1212/wnl.46.4.907
6. Dilokthornsakul P, Valuck RJ, Nair KV, Corboy JR, Allen RR, Campbell JD. Multiple sclerosis prevalence in the United States commercially insured population. *Neurology*. 2016;86(11):1014-1021. doi:10.1212/WNL.0000000000002469
7. Noonan C, Williamson D, Henry J, et al. The Prevalence of Multiple Sclerosis in 3 US Communities. *Public Health Research, Practice, and Policy*. 2010;7(1):1-8.
8. Le Page E, Veillard D, Laplaud DA, et al. Oral versus intravenous high-dose methylprednisolone for treatment of relapses in patients with multiple sclerosis (COPOUSEP): a randomised, controlled, double-blind, non-inferiority trial. *The Lancet*. 2015;386(9997):974-981. doi:10.1016/S0140-6736(15)61137-0
9. Ebers GC, Traboulsee A, Li D, et al. Analysis of clinical outcomes according to original treatment groups 16 years after the pivotal IFNB-1b trial. *J Neurol Neurosurg Psychiatry*. 2010;81(8):907-912. doi:10.1136/jnnp.2009.204123
10. Bornstein MB, Miller A, Slagle S, et al. A pilot trial of Cop 1 in exacerbating-relapsing multiple sclerosis. *N Engl J Med*. 1987;317(7):408-414. doi:10.1056/NEJM198708133170703
11. Aharoni R, Teitelbaum D, Sela M, Arnon R. Copolymer 1 induces T cells of the T helper type 2 that crossreact with myelin basic protein and suppress experimental autoimmune

encephalomyelitis. *Proc Natl Acad Sci U S A*. 1997;94(20):10821-10826.
doi:10.1073/pnas.94.20.10821

12. Scolding N, Barnes D, Cader S, et al. Association of British Neurologists: revised (2015) guidelines for prescribing disease-modifying treatments in multiple sclerosis. *Pract Neurol*. 2015;15(4):273-279. doi:10.1136/practneurol-2015-001139
13. Andersen O. Multicentre, randomised, double blind, placebo controlled, phase III study of weekly, low dose, subcutaneous interferon beta-1a in secondary progressive multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2004;75(5):706-710.
doi:10.1136/jnnp.2003.010090
14. Liao M-F, Yen S-C, Chun-Yen L, Rong-Kuo L. Delayed Liver Function Impairment Secondary to Interferon β -1a Use in Multiple Sclerosis. *Case Rep Neurol*. 2013;5(2):130-134.
doi:10.1159/000354042
15. Long-term safety of natalizumab for treating multiple sclerosis. Mayo Clinic.
<https://www.mayoclinic.org/diseases-conditions/multiple-sclerosis/expert-answers/long-term-safety-natalizumab-for-multiple-sclerosis/faq-20110762>. Accessed November 11, 2019.
16. Mirzaei F, Michels KB, Munger K, et al. Gestational vitamin D and the risk of multiple sclerosis in offspring. *Ann Neurol*. 2011;70(1):30-40. doi:10.1002/ana.22456
17. Kimball SM, Ursell MR, O'Connor P, Vieth R. Safety of vitamin D3 in adults with multiple sclerosis. *Am J Clin Nutr*. 2007;86(3):645-651. doi:10.1093/ajcn/86.3.645
18. Nordvik I, Myhr KM, Nyland H, Bjerve KS. Effect of dietary advice and n-3 supplementation in newly diagnosed MS patients. *Acta Neurol Scand*. 2000;102(3):143-149.
doi:10.1034/j.1600-0404.2000.102003143.x
19. Tettey P, Simpson S, Taylor B, et al. An adverse lipid profile and increased levels of adiposity significantly predict clinical course after a first demyelinating event. *J Neurol Neurosurg Psychiatry*. 2017;88(5):395-401. doi:10.1136/jnnp-2016-315037
20. Weinstock-Guttman B, Zivadinov R, Horakova D, et al. Lipid profiles are associated with lesion formation over 24 months in interferon- β treated patients following the first demyelinating event. *J Neurol Neurosurg Psychiatry*. 2013;84(11):1186-1191.
doi:10.1136/jnnp-2012-304740
21. Sedaghat F, Jessri M, Behrooz M, Mirghotbi M, Rashidkhani B. Mediterranean diet adherence and risk of multiple sclerosis: a case-control study. *Asia Pac J Clin Nutr*. 2016;25(2):377-384. doi:10.6133/apjcn.2016.25.2.12

22. Kampman MT, Wilsgaard T, Mellgren SI. Outdoor activities and diet in childhood and adolescence relate to MS risk above the Arctic Circle. *J Neurol*. 2007;254(4):471-477. doi:10.1007/s00415-006-0395-5
23. Munger KL, Zhang SM, O'Reilly E, et al. Vitamin D intake and incidence of multiple sclerosis. *Neurology*. 2004;62(1):60-65. doi:10.1212/01.WNL.0000101723.79681.38
24. Hoare S, Lithander F, van der Mei I, et al. Higher intake of omega-3 polyunsaturated fatty acids is associated with a decreased risk of a first clinical diagnosis of central nervous system demyelination: Results from the Ausimmune Study. *Mult Scler J*. 2016;22(7):884-892. doi:10.1177/1352458515604380
25. Kouchaki E, Afarini M, Abolhassani J, et al. High-dose ω -3 Fatty Acid Plus Vitamin D3 Supplementation Affects Clinical Symptoms and Metabolic Status of Patients with Multiple Sclerosis: A Randomized Controlled Clinical Trial. *J Nutr*. 2018;148(8):1380-1386. doi:10.1093/jn/nxy116
26. Weinstock-Guttman B, Baier M, Park Y, et al. Low fat dietary intervention with omega-3 fatty acid supplementation in multiple sclerosis patients. *Prostaglandins Leukot Essent Fatty Acids*. 2005;73(5):397-404. doi:10.1016/j.plefa.2005.05.024
27. Burton JM, Kimball S, Vieth R, et al. A phase I/II dose-escalation trial of vitamin D3 and calcium in multiple sclerosis. *Neurology*. 2010;74(23):1852-1859. doi:10.1212/WNL.0b013e3181e1cec2
28. Office of Dietary Supplements - Vitamin D. <https://ods.od.nih.gov/factsheets/VitaminD-Consumer/>. Accessed November 21, 2019.
29. Buckley LM. Calcium and Vitamin D₃ Supplementation Prevents Bone Loss in the Spine Secondary to Low-Dose Corticosteroids in Patients with Rheumatoid Arthritis: A Randomized, Double-Blind, Placebo-Controlled Trial. *Ann Intern Med*. 1996;125(12):961. doi:10.7326/0003-4819-125-12-199612150-00004