

Komplementäre und alternative Therapien der multiplen Sklerose

Stefan Schwarz, Hans Leweling, Bernd-Udo Sagstetter, Mannheim, und Hans-Michael Meinck, Heidelberg

Literatur

1. Deutsche Gesellschaft für Ernährung (DGE) (1999). Tipps der Deutschen Gesellschaft für Ernährung e.V. zur Ernährung bei Multipler Sklerose. <http://www.dge.de/modules.php?name=News&file=article&sid=60>, accessed 03.11.2007.
2. Seviton MS (2007) <http://www.seviton.de>, accessed 14.11.2007.
3. Defining and describing complementary and alternative medicine. Panel on definition and description. CAM Research Methodology Conference, April 1995. *Altern Ther Health Med* 1997;3:49–57.
4. Multiple Sklerose Therapie Konsensus Gruppe (MSTKG). Symptomatische Therapie der Multiplen Sklerose. *Nervenarzt* 2004;75(Suppl 1):2–39.
5. National Institutes of Health State-of-the-Science Conference Statement: multivitamin/mineral supplements and chronic disease prevention. *Am J Clin Nutr* 2007;85:257S–64S.
6. Aminzadeh KK, Etmann M. Dental amalgam and multiple sclerosis: a systematic review and meta-analysis. *J Public Health Dent* 2007;67:64–6.
7. Antonovsky A, Leibowitz U, Smith HA. Epidemiologic study of multiple sclerosis in Israel. I. An overall review of methods and findings. *Arch Neurol* 1965;13:183–93.
8. Apel A, Greim B, König N, et al. Frequency of current utilisation of complementary and alternative medicine by patients with multiple sclerosis. *J Neurol* 2006;253:1331–6.
9. Apel A, Greim B, Zettl UK. Complementary and alternative medicine and coping in neuroimmunological diseases. *J Neurol* 2007;254(Suppl 2):112–5.
10. Baker D, Pryce G, Croxford JL, et al. Cannabinoids control spasticity and tremor in a multiple sclerosis model. *Nature* 2000;404:84–7.
11. Barnes MP. Sativex: clinical efficacy and tolerability in the treatment of symptoms of multiple sclerosis and neuropathic pain. *Expert Opin Pharmacother* 2006;7:607–15.
12. Bates D, Cartledge NE, French JM, et al. A double-blind controlled trial of long chain n-3 polyunsaturated fatty acids in the treatment of multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1989;52:18–22.
13. Bates D, Fawcett PR, Shaw DA, et al. Polyunsaturated fatty acids in treatment of acute relapsing multiple sclerosis. *Br Med J* 1978;2:1390–1.
14. Baumhackl U, Kappos L, Radue EW, et al. A randomized, double-blind, placebo-controlled study of oral hydrolytic enzymes in relapsing multiple sclerosis. *Mult Scler* 2005;11:166–8.
15. Bennett M, Heard R. Hyperbaric oxygen therapy for multiple sclerosis. *Cochrane Database Syst Rev* 2004:CD003057.
16. Berr C, Puel J, Clanet M, et al. Risk factors in multiple sclerosis: a population-based case-control study in Hautes-Pyrénées, France. *Acta Neurol Scand* 1989;80:46–50.
17. Bjelakovic G, Nikolova D, Simonetti RG, et al. Antioxidant supplements for prevention of gastrointestinal cancers: a systematic review and meta-analysis. *Lancet* 2004;364:1219–28.
18. Bowling AC, Stewart TM. Current complementary and alternative therapies for multiple sclerosis. *Curr Treat Options Neurol* 2003;5:55–68.
19. Brenneisen R, Egli A, Elshohly MA, et al. The effect of orally and rectally administered delta 9-tetrahydrocannabinol on spasticity: a pilot study with 2 patients. *Int J Clin Pharmacol Ther* 1996;34:446–52.
20. Brochet B, Guinot P, Orgogozo JM, et al. Double blind placebo controlled multicentre study of ginkgolide B in treatment of acute exacerbations of multiple sclerosis. The Ginkgolide Study Group in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1995;58:360–2.
21. Cader S, Cifelli A, Abu-Omar Y, et al. Reduced brain functional reserve and altered functional connectivity in patients with multiple sclerosis. *Brain* 2006;129:527–37.
22. Calabresi PA. Considerations in the treatment of relapsing-remitting multiple sclerosis. *Neurology* 2002;58:S10–22.
23. Calder PC. Dietary fatty acids and the immune system. *Lipids* 1999;34(34 Suppl):137S–40S.
24. Calder PC. Polyunsaturated fatty acids, inflammation, and immunity. *Lipids* 2001;36:1007–24.
25. Cantorna M, Humpal-Winter J, DeLuca H. In vivo upregulation of interleukin-4 is one mechanism underlying the immunoregulatory effects of 1,25-dihydroxyvitamin D3. *Arch Biochem Biophys* 2000;377:135–8.
26. Cantorna MT, Hayes CE, DeLuca HF. 1,25-dihydroxyvitamin D3 reversibly blocks the progression of relapsing encephalomyelitis, a model of multiple sclerosis. *Proc Natl Acad Sci* 1996;93:7861–4.
27. Carder PC, Vuckovic N, Green CA. Negotiating medications: patient perceptions of long-term medication use. *J Clin Pharm Ther* 2003;28:409–17.
28. Casetta I, Invernizzi M, Granieri E. Multiple sclerosis and dental amalgam: case-control study in Ferrara, Italy. *Neuroepidemiology* 2001;20:134–7.

Prof. Dr. med. Stefan Schwarz, Zenralinstitut für Seelische Gesundheit, Universität Heidelberg, J5, 68159 Mannheim, E-mail: st_schwarz@hotmail.com
 Priv.-Doz. Dr. med. Hans Leweling, IV. Medizinische Klinik, Universitätsklinikum Mannheim GmbH, Medizinische Fakultät der Universität Heidelberg, Theodor-Kutzer-Ufer 1–3, 68135 Mannheim
 Bernd-Udo Sagstetter, Apotheke des Universitätsklinikums Mannheim GmbH, Medizinische Fakultät der Universität Heidelberg, Theodor-Kutzer-Ufer 1–3, 68135 Mannheim
 Prof. Dr. med. Hans-Michael Meinck, Neurologische Klinik, Klinikum Heidelberg der Universität Heidelberg, Im Neuenheimer Feld 400, 69120 Heidelberg

29. Chong MS, Wolff K, Wise K, et al. Cannabis use in patients with multiple sclerosis. *Mult Scler* 2006;12:646–51.
30. Clark AJ, Ware MA, Yazer E, et al. Patterns of cannabis use among patients with multiple sclerosis. *Neurology* 2004;62:2098–2100.
31. Clausen J, Moller J. Experimental allergic encephalomyelitis provoked in rats after developmental lack of polyunsaturated fatty acids. *Acta Neurol Scand* 1967;43(Suppl 31):74.
32. Clifford DB. Tetrahydrocannabinol for tremor in multiple sclerosis. *Ann Neurol* 1983;13:669–71.
33. Coo H, Aronson KJ. A systematic review of several potential non-genetic risk factors for multiple sclerosis. *Neuroepidemiology* 2004;23:1–12.
34. Cosman F, Nieves J, Komar L, et al. Fracture history and bone loss in patients with MS. *Neurology* 1998;51:1161–5.
35. de Lago E, Ligresti A, Ortar G, et al. In vivo pharmacological actions of two novel inhibitors of anandamide cellular uptake. *Eur J Pharmacol* 2004;484:249–57.
36. DeFeudis FV, Drieu K. Ginkgo biloba extract (EGb 761) and CNS functions: basic studies and clinical applications. *Curr Drug Targets* 2000;1:25–58.
37. Dworkin RH, Bates D, Millar JH, et al. Linoleic acid and multiple sclerosis: a reanalysis of three double-blind trials. *Neurology* 1984;34:1441–5.
38. Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990–1997: results of a follow-up national survey. *Jama* 1998;280:1569–75.
39. Ernst E. Harmless herbs? A review of the literature. *Am J Med* 1998;104:170–8.
40. Filippini G, Brusafferri F, Sibley WA, et al. Corticosteroids or ACTH for acute exacerbations in multiple sclerosis. *Cochrane Database Syst Rev* 2000;CD001331.
41. Filippini G, Munari L, Incorvaia B, et al. Interferons in relapsing remitting multiple sclerosis: a systematic review. *Lancet* 2003;361:545–52.
42. Fischer BH, Marks M, Reich T. Hyperbaric-oxygen treatment of multiple sclerosis. A randomized, placebo-controlled, double-blind study. *N Engl J Med* 1983;308:181–6.
43. Fisher AA, Le Couteur DG. Lead poisoning from complementary and alternative medicine in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2000;69:687–9.
44. Fleming JO, Hummel AL, Beinlich BR, et al. Vitamin D treatment of relapsing-remitting multiple sclerosis (RRMS): a MRI-based pilot study. *Neurology* 2000;54:A338.
45. Fox P, Bain PG, Glickman S, et al. The effect of cannabis on tremor in patients with multiple sclerosis. *Neurology* 2004;62:1105–9.
46. Ghezzi A, Zaffaroni M. Neurological manifestations of gastrointestinal disorders, with particular reference to the differential diagnosis of multiple sclerosis. *Neurol Sci* 2001;22(Suppl 2):S117–22.
47. Gilgun-Sherki Y, Melamed E, Offen D. The role of oxidative stress in the pathogenesis of multiple sclerosis: The need for effective antioxidant therapy. *J Neurol* 2004;251:261–8.
48. Göbel HH, Walthert G, Meuth M. Fresh cell therapy followed by fatal coma. *J Neurol* 1986;233:242–7.
49. Goldberg P, Fleming MC, Picard EH. Multiple sclerosis: decreased relapse rate through dietary supplementation with calcium, magnesium and vitamin D. *Med Hypotheses* 1986;21:193–200.
50. Goodkin DE, Jacobsen DW, Galvez N, et al. Serum cobalamin deficiency is uncommon in multiple sclerosis. *Arch Neurol* 1994;51:1110–4.
51. Gusev E, Boiko A, Lauer K, et al. Environmental risk factors in MS: a case-control study in Moscow. *Acta Neurol Scand* 1996;94:386–94.
52. Hall W, Solowij N. Adverse effects of cannabis. *Lancet* 1998;352:1611–6.
53. Harbige LS. Dietary n-6 and n-3 fatty acids in immunity and autoimmune disease. *Proc Nutr Soc* 1998;57:555–62.
54. Harbige LS. Fatty acids, the immune response, and autoimmunity: a question of n-6 essentiality and the balance between n-6 and n-3. *Lipids* 2003;38:323–41.
55. Harbige LS, Layward L, Morris-Downes MM, et al. The protective effects of omega-6 fatty acids in experimental autoimmune encephalomyelitis (EAE) in relation to transforming growth factor-beta 1 (TGF-beta1) up-regulation and increased prostaglandin E2 (PGE2) production. *Clin Exp Immunol* 2000;122:445–52.
56. Harbige LS, Yeatman N, Amor S, et al. Prevention of experimental autoimmune encephalomyelitis in Lewis rats by a novel fungal source of gamma-linolenic acid. *Br J Nutr* 1995;74:701–15.
57. Hayes CE, Nashold FE, Spach KM, et al. The immunological functions of the vitamin D endocrine system. *Cell Mol Biol* 2003;49:277–300.
58. Henze T, Rieckmann P, Toyka KV. Symptomatic treatment of multiple sclerosis. Multiple Sclerosis Therapy Consensus Group (MSTCG) of the German Multiple Sclerosis Society. *Eur Neurol* 2006;56:78–105.
59. Herndon R, Mohandas N. Osteoporosis in multiple sclerosis: a frequent, serious, and under-recognized problem. *Int J MS Care* 2000;2:5.
60. Huntley A. A review of the evidence for efficacy of complementary and alternative medicines in MS. *Int MS J* 2006;13:5-12, 14, 2006.
61. Iskedjian M, Bereza B, Gordon A, et al. Meta-analysis of cannabis based treatments for neuropathic and multiple sclerosis-related pain. *Curr Med Res Opin* 2007;23:17–24.
62. James PB. Evidence for subacute fat embolism as the cause of multiple sclerosis. *Lancet* 1982;1:380–6.
63. Jensen C, Clausen J. Glutathione peroxidase activity, associated enzymes and substrates in blood cells from patients with multiple sclerosis – effects of antioxidant supplementation. *Acta Pharmacol Toxicol (Copenh)* 1986;59(Suppl 7):450–3.
64. Jensen GE, Gissel-Nielsen G, Clausen J. Leucocyte glutathione peroxidase activity and selenium level in multiple sclerosis. *J Neurol Sci* 1980;48:61–7.
65. Jimenez-Jimenez FJ, de Bustos F, Molina JA, et al. Cerebrospinal fluid levels of alpha-tocopherol in patients with multiple sclerosis. *Neurosci Lett* 1998;249:65–7.
66. Johns A. Psychiatric effects of cannabis. *Br J Psychiatry* 2001;178:116–22.
67. Johnson SK, Diamond BJ, Rausch S, et al. The effect of Ginkgo biloba on functional measures in multiple sclerosis: a pilot randomized controlled trial. *Explore (NY)* 2006;2:19–24.
68. Killestein J, Hoogervorst EL, Reif M, et al. Safety, tolerability, and efficacy of orally administered cannabinoids in MS. *Neurology* 2002;58:1404–7.
69. Kira J, Tobimatsu S, Goto I. Vitamin B12 metabolism and massive-dose methyl vitamin B12 therapy in Japanese patients with multiple sclerosis. *Intern Med* 1994;33:82–6.
70. Kleijnen J, Knipschild P. Hyperbaric oxygen for multiple sclerosis. Review of controlled trials. *Acta Neurol Scand* 1995;91:330–4.
71. Kotynek M. Haschisch aus dem Panzerschrank. *Sueddtsch Zeitung* 22. August 2007.
72. Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation* 2002;106:2747–57.
73. Lauer K. Diet and multiple sclerosis. *Neurology* 1997;49:S55–61.
74. Lauer K, Firnhaber W. An evaluation of laboratory investigations in patients with multiple sclerosis. *J Chronic Dis* 1986;39:767–74.
75. Linde K, Witt CM, Streng A, et al. The impact of patient expectations on outcomes in four randomized controlled trials of acupuncture in patients with chronic pain. *Pain* 2007;128:264–71.
76. Lovera J, Bagert B, Smoot K, et al. Ginkgo biloba for the improvement of cognitive performance in multiple sclerosis: a randomized, placebo-controlled trial. *Mult Scler* 2007;13:376–85.
77. Luthra YK, Rosenkrantz H. Cannabinoids: neurochemical aspects after oral chronic administration to rats. *Toxicol Appl Pharmacol* 1974;27:158–68.
78. Marrie RA, Hadjimichael O, Vollmer T. Predictors of alternative medicine use by multiple sclerosis patients. *Mult Scler* 2003;9:461–6.
79. Mazzella GL, Sinfiorani E, Savoldi F, et al. Blood cells glutathione peroxidase activity and selenium in multiple sclerosis. *Eur Neurol* 1983;22:442–6.
80. Meade CJ, Mertin J, Sheena J, et al. Reduction by linoleic acid of the severity of experimental allergic encephalomyelitis in the guinea pig. *J Neurol Sci* 1978;35:291–308.
81. Meinck HM, Schonle PW, Conrad B. Effect of cannabinoids on spasticity and ataxia in multiple sclerosis. *J Neurol* 1989;236:120–2.
82. Millar JH, Zilkha KJ, Langman MJ, et al. Double-blind trial of linoleate supplementation of the diet in multiple sclerosis. *Br Med J* 1973;1:765–8.
83. Moreau T, Loudonot V. Dental amalgam and multiple sclerosis: what is the connection? *Presse Med* 1999;28:1378–80.
84. Munger KL, Zhang SM, O'Reilly E, et al. Vitamin D intake and incidence of multiple sclerosis. *Neurology* 2004;62:60–5.

85. Nashold FE, Miller DJ, Hayes CE. 1,25-dihydroxyvitamin D₃ treatment decreases macrophage accumulation in the CNS of mice with experimental autoimmune encephalomyelitis. *J Neuroimmunol* 2000;103:171–9.
86. Nayak S, Matheis RJ, Schoenberger NE, et al. Use of unconventional therapies by individuals with multiple sclerosis. *Clin Rehabil* 2003;17:181–91.
87. Neiman J, Nilsson BY, Barr PO, et al. Hyperbaric oxygen in chronic progressive multiple sclerosis: visual evoked potentials and clinical effects. *J Neurol Neurosurg Psychiatry* 1985;48:497–500.
88. Nieves J, Cosman F, Herbert J, et al. High prevalence of vitamin D deficiency and reduced bone mass in multiple sclerosis. *Neurology* 1994;44:1687–92.
89. Nordvik I, Myhr KM, Nyland H, et al. Effect of dietary advice and n-3 supplementation in newly diagnosed MS patients. *Acta Neurol Scand* 2000;102:143–9.
90. Notcutt W, Price M, Miller R, et al. Initial experiences with medicinal extracts of cannabis for chronic pain: results from 34 'N of 1' studies. *Anaesthesia* 2004;59:440–52.
91. O'Connor JS, Davis RL, Langworthy OR, et al. B12 metabolism and multiple sclerosis. *Proc Soc Exp Biol Med* 1960;103:180–3.
92. Oriani G, Barbieri S, Cislighi G, et al. Long-term hyperbaric oxygen in multiple sclerosis: a placebo-controlled, double blind trial with evoked potential studies. *J Hyperbaric Med* 1990;5:237–45.
93. Page SA, Verhoef MJ, Stebbins RA, et al. Cannabis use as described by people with multiple sclerosis. *Can J Neurol Sci* 2003;30:201–5.
94. Page SA, Verhoef MJ, Stebbins RA, et al. The use of complementary and alternative therapies by people with multiple sclerosis. *Chronic Dis Can* 2003;24:75–9.
95. Paty DW, Cousin HK, Read S, et al. Linoleic acid in multiple sclerosis: failure to show any therapeutic benefit. *Acta Neurol Scand* 1978;58:53–8.
96. Petro DJ, Ellenberger C Jr. Treatment of human spasticity with delta 9-tetrahydrocannabinol. *J Clin Pharmacol* 1981;21(8-9 Suppl):413S–6S.
97. Pryce G, Ahmed Z, Hankey DJ, et al. Cannabinoids inhibit neurodegeneration in models of multiple sclerosis. *Brain* 2003;126:2191–202.
98. Pucci E, Cartechini E, Taus C, et al. Why physicians need to look more closely at the use of complementary and alternative medicine by multiple sclerosis patients. *Eur J Neurol* 2004;11:263–7.
99. Reynolds EH. Multiple sclerosis and vitamin B12 metabolism. *J Neuroimmunol* 1992;40:225–30.
100. Reynolds EH, Linnell JC. Vitamin B12 deficiency, demyelination, and multiple sclerosis. *Lancet* 1987;2:920.
101. Reynolds EH, Linnell JC, Faludy JE. Multiple sclerosis associated with vitamin B12 deficiency. *Arch Neurol* 1991;48:808–11.
102. Rieckmann P, Toyka KV, Bassetti C, et al. Escalating immunotherapy of multiple sclerosis – new aspects and practical application. *J Neurol* 2004;251:1329–39.
103. Roesler J, Emmendorffer A, Steinmuller C, et al. Application of purified polysaccharides from cell cultures of the plant *Echinacea purpurea* to test subjects mediates activation of the phagocyte system. *Int J Immunopharmacol* 1991;13:931–41.
104. Rog DJ, Nurmikko TJ, Friede T, et al. Randomized, controlled trial of cannabis-based medicine in central pain in multiple sclerosis. *Neurology* 2005;65:812–9.
105. Sandyk R, Awerbuch GI. Vitamin B12 and its relationship to age of onset of multiple sclerosis. *Int J Neurosci* 1993;71:93–9.
106. Schwartz CE, Laitin E, Brotman S, et al. Utilization of unconventional treatments by persons with MS: is it alternative or complementary? *Neurology* 1999;52:626–9.
107. Schwarz S, Knauth N, Schwab S, et al. Acute disseminated encephalomyelitis after parenteral therapy with herbal extracts: a report of two cases. *J Neurol Neurosurg Psychiatry* 2000;69:516–8.
108. Schwarz S, Knorr C, Geiger H, Flachenecker P. Use of alternative and complementary medicine (CAM) in 1 573 patients with multiple sclerosis (MS). *Mult Scler* 2007;13:S89.
109. Schwarz S, Leweling H. Ernährung und Multiple Sklerose. *Nervenarzt* 2005;76:131–42.
110. Schwarz S, Leweling H. Multiple sclerosis and nutrition. *Mult Scler* 2005;11:24–32.
111. Shabas D, Weinreb H. Preventive healthcare in women with multiple sclerosis. *J Womens Health Gend Based Med* 2000;9:389–95.
112. Shakespeare D, Boggild M, Young C. Anti-spasticity agents for multiple sclerosis. *Cochrane Database Syst Rev* 2003;4:CD001332.
113. Sharts-Hopko NC, Sullivan MP. Beliefs, perceptions, and practices related to osteoporosis risk reduction among women with multiple sclerosis. *Rehabil Nurs* 2002;27:232–6.
114. Shinto L, Yadav V, Morris C, et al. The perceived benefit and satisfaction from conventional and complementary and alternative medicine (CAM) in people with multiple sclerosis. *Complement Ther Med* 2005;13:264–72.
115. Simone IL, Ceccarelli A, Tortorella C, et al. Influence of interferon beta treatment on quality of life in multiple sclerosis patients. *Health Qual Life Outcomes* 2006;4:96.
116. Simpson CA. Vitamin B12 levels in the serum and cerebrospinal fluid in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1964;27:174–7.
117. Simson G, Herfort A, Krim M, et al. Effects of vitamin B12 in multiple sclerosis. *Proc Soc Exp Biol Med* 1950;75:721.
118. Sjöstrom PJ, Turrigiano GG, Nelson SB. Neocortical LTD via coincident activation of presynaptic NMDA and cannabinoid receptors. *Neuron* 2003;39:641–54.
119. Smelzer S, Zimmerman V, Capriotti T. Osteoporosis risk factors and bone mineral density in women with MS. *Int J MS Care* 2000;4:17–29.
120. Smith DK, Feldman EB, Feldman DS. Trace element status in multiple sclerosis. *Am J Clin Nutr* 1989;50:136–40.
121. Somerset M, Campbell R, Sharp DJ, et al. What do people with MS want and expect from health-care services? *Health Expect* 2001;4:29–37.
122. Stewart TM, Bowling AC. Polyunsaturated fatty acid supplementation in MS. *Int MS J* 2005;12:88–93.
123. Stranges S, Marshall JR, Natarajan R, et al. Effects of long-term selenium supplementation on the incidence of type 2 diabetes: a randomized trial. *Ann Intern Med* 2007;147:217–23.
124. Svendsen KB, Jensen TS, Bach FW. Does the cannabinoid dronabinol reduce central pain in multiple sclerosis? Randomised double blind placebo controlled crossover trial. *BMJ* 2004;329:253.
125. Swank RL. Treatment of multiple sclerosis with a low-fat diet. *J Am Diet Assoc* 1960;36:322–5.
126. Swank RL, Bourdillon RB. Multiple sclerosis: assessment of treatment with a modified low-fat diet. *J Neurochem* 1960;131:468–88.
127. Swank RL, Dugan BB. Effect of low saturated fat diet in early and late cases of multiple sclerosis. *Lancet* 1990;336:37–9.
128. Tang BM, Eslick GD, Nowson C, et al. Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. *Lancet* 2007;370:657–66.
129. Tibbles PM, Edelsberg JS. Hyperbaric-oxygen therapy. *N Engl J Med* 1996;334:1642–8.
130. Tramèr MR, Carroll C, Campbell FA, et al. Cannabinoids for control of chemotherapy induced nausea and vomiting: quantitative systematic review. *BMJ* 2001;323:1–8.
131. Ungerleider JT, Andrysiak T, Fairbanks L, et al. Delta-9-THC in the treatment of spasticity associated with multiple sclerosis. *Adv Alcohol Subst Abuse* 1987;7:39–50.
132. van der Ploeg HM, Molenaar MJ, van Tiggelen CW. Use of alternative treatments by patients with multiple sclerosis. *Ned Tijdschr Geneesk* 1994;138:296–9.
133. van Etten E, Branisteanu DD, Verstuyf A, et al. Analogs of 1,25-dihydroxyvitamin D₃ as dose-reducing agents for classical immunosuppressants. *Transplantation* 2000;69:1932–42.
134. Vieth R. Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety. *Am J Clin Nutr* 1999;69:842–56.
135. Wade DT, Makela P, Robson P, et al. Do cannabis-based medicinal extracts have general or specific effects on symptoms in multiple sclerosis? A double-blind, randomized, placebo-controlled study on 160 patients. *Mult Scler* 2004;10:434–41.
136. Wade DT, Makela PM, House H, et al. Long-term use of a cannabis-based medicine in the treatment of spasticity and other symptoms in multiple sclerosis. *Mult Scler* 2006;12:639–45.
137. Wade DT, Robson P, House H, et al. A preliminary controlled study to determine whether whole-plant cannabis extracts can improve intractable neurogenic symptoms. *Clin Rehabil* 2003;17:21–9.
138. Wade DT, Young CA, Chaudhuri KR, et al. A randomised placebo controlled exploratory study of vitamin B₁₂, lofepramine, and L-phenyl-

- alanine (the "Cari Loder regime") in the treatment of multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2002;73:246–9.
139. Walther EU, Hohlfeld R. Multiple sclerosis: side effects of interferon beta therapy and their management. *Neurology* 1999;53:1622–7.
 140. Werneke U, Turner T, Priebe S. Complementary medicines in psychiatry: review of effectiveness and safety. *Br J Psychiatry* 2006;188:587.
 141. Wikstrom J, Westermarck T, Palo J. Selenium, vitamin E and copper in multiple sclerosis. *Acta Neurol Scand* 1976;54:287–90.
 142. Winterholler M. Durch den Dschungel der alternativen Heilverfahren. *Aktiv (Zeitschrift der Deutschen Multiple Sklerose Gesellschaft DSMG)* 1999;183:8–10, abrufbar unter <http://www.dsmg.de>
 143. Winterholler M, Erbguth F, Neundörfer B. Verwendung paramedizinischer Verfahren durch MS-Patienten – Patientencharakterisierung und Anwendungsgewohnheiten. *Fortschr Neurol Psychiatr* 1997;65:555–61.
 144. Wirguin I, Mechoulam R, Breuer A, et al. Suppression of experimental autoimmune encephalomyelitis by cannabinoids. *Immunopharmacology* 1994;28:209–14.
 145. Yip HK, Li DK, Yau DC. Dental amalgam and human health. *Int Dent J* 2003;53:464–8.
 146. Zajicek J, Fox P, Sanders H, et al. Cannabinoids for treatment of spasticity and other symptoms related to multiple sclerosis (CAMS study): multicentre randomised placebo-controlled trial. *Lancet* 2003;362:1517–26.
 147. Zajicek JP, Sanders HP, Wright DE, et al. Cannabinoids in multiple sclerosis (CAMS) study: safety and efficacy data for 12 months follow up. *J Neurol Neurosurg Psychiatry* 2005;76:1664–9.
 148. Zhang SM, Hernan MA, Olek MJ, et al. Intakes of carotenoids, vitamin C, and vitamin E and MS risk among two large cohorts of women. *Neurology* 2001;57:75–80.
 149. Zhang SM, Willett WC, Hernan MA, et al. Dietary fat in relation to risk of multiple sclerosis among two large cohorts of women. *Am J Epidemiol* 2000;152:1056–64.
 150. Zollman C, Vickers A. What is complementary medicine? *BMJ* 1999;319:693–6.