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# Multiple sclerosis and nutrition

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***Benefits from any particular diet in multiple sclerosis (MS) have not yet been proven. It is, however, frequent that malnutrition may potentially exacerbate the symptoms of MS. There is some evidence that a high intake of saturated fat increases the incidence of MS. Epidemiological studies imply that unsaturated fatty acids may have a positive effect on the course of MS. However, the results of controlled studies are ambiguous. A meta-analysis of three small controlled clinical trials suggests a benefit from linoleic acid. Intake of Vitamin D is associated with a lower incidence of MS. In MS, the risk of osteoporosis is high, and prophylactic vitamin D and calcium should be considered at an early stage. The role of minerals, trace elements, antioxidants, vitamins or fish oil is unclear. The possible relationships between diet and MS have not been subjected to adequate study. It seems possible that in the future, diets or dietary supplements may become recommended forms of treatment for MS.***
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## *Introduction*

Publications on multiple sclerosis (MS) tend to begin almost ritually with the notion that the possibilities available to modern medicine have been revolutionized during the last decade and that today a wide range of effective treatments are available. Many patients, however, perceive the reality differently: they are suffering from a disease of unknown origin, which cannot be healed; whose symptoms are difficult to treat, and whose course, despite all of the medical measures taken, frequently and inexorably worsens. It is, therefore, almost inevitable that many patients turn to alternative therapies for help. The majority of MS patients employ a variety of alternative therapies, and diet or dietary supplements constitute a large proportion of these measures.[1,2] The main motive is not a general mistrust of medical science, but an understandable desire to try anything which might seem to offer the patient some hope of recovery. Moreover, complicated, time-consuming diets or other adjustments in lifestyle may provide a sense of control and initiative, restraining the feeling of being helplessly exposed to a mysterious disease.[1] Such needs are largely ignored by the medical profession at large and create a breeding ground for profit-oriented doctors and other healers.

Although no specific benefit from a particular diet has been proven, numerous experimental, epidemiological and clinical studies suggest that nutritional factors may influence the incidence as well as the course of the disease. With this review, we intend to provide a brief overview of the epidemiological studies on diet and the incidence of MS and to discuss the possible effects of particular diets and dietary supplements.

## *Diet as a possible risk factor for MS*

The first clinical descriptions of MS date back to the end of the 19th century. Because of its distinctive clinical characteristics, it may be assumed that the disease was essentially nonexistent previous to that time. The incidence of MS is strikingly related to geographic latitude and generally increases with the distance from the equator.[3,4] Dietary factors have repeatedly been suggested as a possible explanation for this phenomenon. However, there is, as yet, no definite proof that diet actually influences the incidence of MS.[4]

Methodological problems complicate investigations on the correlation between diet and multiple sclerosis. There are only a few prospective ecological studies available and most evidence is derived from case-control or population-based epidemiological studies. Population-based epidemiological studies indicate a variety of associations between MS and diet.[4,5] More than 50 years ago, Swank *et al.* analysed the incidence of MS in geographically diverse regions in Norway.[6] They found a

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higher incidence in the inland areas compared with the coastal regions where the intake of fish was higher and the consumption of saturated animal fat was lower. In the USA, Agranoff and Goldberg linked the incidence of MS to geographic latitude and dietary habits.[7] High consumption of milk and low average ambient temperatures were associated with a high incidence, whereas the intake of fish and unsaturated fat seemed to be of a preventive nature. Alter *et al*. analysed epidemiological data from 22 countries.[3] The prevalence of MS correlated positively with the intake of total energy, fat, oil and protein. Above all, the intake of animal fat was associated with the prevalence of MS (a correlation coefficient of 0.7). Knox analysed mortality statistics from 20 countries.[6] Mortality from MS correlated with the consumption of a variety of foodstuffs of animal origin (meat, milk, butter, eggs) and refined sugar. The strongest correlation was with the total fat intake. Butcher studied the association between the consumption of milk and the prevalence of MS.[9] He found regional correlations as well as temporal changes related to the consumption of milk. For example, the incidence of MS in Japan rose between 1950 and 1969 in parallel with increased consumption of milk. Lauer *et al*. evaluated the incidence of MS in numerous states of the USA.[10] The intake of meat, dairy products and low average temperatures were each independently associated with the incidence of MS. Esparza *et al*. confirmed these results.[11] In their analyses of epidemiological data from 38 countries, a high intake of animal fat and geographic latitude were related to the incidence of MS. In summary, most population-based epidemiological studies suggest an association between the incidence of MS and the intake of saturated fat of animal origin.

However, these findings are not confirmed by the majority of the population-based case-control studies which have failed to identify a relationship between the intake of fat or meat and the incidence of MS.[12–16] Only a few case control studies found any association between the incidence of MS and the intake of meat, fat of animal origin, saturated fat or dairy products.[17–19] The case-control studies have yielded mixed results (overview and discussion of the methodological problems see Lauer *et al*.[5]). A large number of differing risk factors were identified including the consumption of brain,[20] sweets and confectionery,[12] young potatoes,[13] alcohol,[14,17] smoked meat products,[17,21] and, in an Italian study, a high intake of *pasta*, bread, horse meat, *minestrone*, coffee and tea.[15] As far as breast feeding is concerned, there have been a number of conflicting results.[22,23] As preventive factors, some individual studies suggest the intake of vitamin D[24] (see below) and a high consumption of vegetables.[19] Remarkably, most studies found no correlation with the consumption of fruit or vegetables.

The evidence from the epidemiological studies is inconsistent and difficult to interpret. Many studies suggest an association between the incidence of MS and the intake of saturated fat of animal origin. However, any causal relationship remains to be proven.

## *Nutritional status in MS patients*

Dietary habits and the nutritional status in MS patients have not been extensively studied. Individual findings and our own experience suggest that many patients suffer from various forms of malnutrition; obesity, weight loss, or vitamin deficiency are not unusual. Studies on the nutritional status in MS depend heavily on the patient group selected. In a population of unselected patients – many of them had been only recently diagnosed and were only slightly or moderately disabled – the nutritional status was comparable with that of the population in general.[25] With severely disabled patients, the proportion of patients suffering from malnutrition and weight loss increases.[26] Hewson *et al*. documented the food intake of 142 patients over seven days.[27] In comparison to a healthy control group, the patients had a smaller intake of calories; however, the composition of the food was no different. Timmerman and Stuifbergen analysed the food intake of women with MS over three days.[28] When compared with current recommendations, the patients consumed an inadequately small amount of carbohydrates, fibres, vitamin E, calcium and zinc. In contrast, their intakes of saturated fat, protein, vitamin A and C, folic acid and iron were greater. The reliability of these studies is limited as the patient groups were heterogeneous, and it can be assumed that only those patients who are relatively moderately disabled or who are in receipt of excellent care participate in trials of this type.[29]

Williams *et al*. examined 20 severely disabled patients; 10 of them suffered from pressure sores.[30] For both groups, the intakes of energy, folic acid, vitamin D, iron and zinc were below recommended values. All of the patients had relatively low levels of albumin, zinc and iron. The patients with pressure sores had significantly lower serum levels of iron and zinc. The authors concluded that the prevalence of malnutrition in severely disabled MS patients is high, and that deficiencies in zinc and iron make them more susceptible to pressure sores. However, in another study, the serum levels of copper, selenium and zinc were within the normal range.[31]

Obesity is frequent in MS patients.[27,28] Immobility and subsequent low energy expenditure, steroids, anti-depressants, and a boring, inactive daily life are amongst the causal factors. On the other hand, obesity and an eating pattern consisting of a few heavy meals per day can aggravate fatigue syndromes, cause complications such as pressure sores or thrombosis, or may worsen disabilities already existing.

With increasing disability, weight loss, malnutrition and cachexia are frequently found.[29,30,32] In addition to MS-specific factors such as dysphagia or adynamia, drugs potentially contribute to the development of malnutrition. Dysphagia is a common and often overlooked symptom in MS patients; its actual prevalence may be underestimated.[25] Baclofen (nausea, sedation), Metoclopramid (diarrhoea) or antibiotics are drugs which typically contribute to lack of appetite.[33] Malnutrition itself can aggravate fatigue, muscular weakness or spasms and is

often neglected as an aetiological cofactor of these common MS symptoms.[29]

To summarize, nutritional imbalances in MS are common and may have a negative effect on the course of the disease, as well as, more importantly, the patient's quality of life. For the individual patient, an interdisciplinary approach including dietary advice, occupational, speech and physical therapy is required.

## Fat and fatty acids

The hypothesis that a modification of the intake of fat might influence the course of MS is derived from pathophysiological considerations, and the results from animal experiments and epidemiological studies suggesting an increased incidence of MS in populations with a high intake of saturated fat. Polyunsaturated fatty acids, in particular, omega-3 fatty acids, produce various immunomodulatory and anti-inflammatory reactions which may influence the course of the disease.[34] Vegetable fats constitute the main source of unsaturated fat.

In the European and North American diet, omega-6 unsaturated fatty acids predominate. Important essential fatty acids from dietary sources are alpha-linolenic acid (omega-3) and linoleic acid (omega-6). To a large extent, omega-3 fatty acids are also derived from eicosanoids (eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)). From these fatty acids, the same enzyme systems synthesize various other unsaturated fatty acids, which serve as the main precursors of leukotrienes and prostaglandins. If the intake of omega-3 fatty acids is increased, they will partially replace the omega-6 fatty acids within the cell membranes.[35] Omega-3 and omega-6 fatty acids are the substrates of identical enzymes for the synthesis of prostaglandins. Therefore, an increased intake of omega-3 fatty acids, e.g. with eicosanoids from fish oil, slows the production of the proinflammatory leukotrienes and prostaglandins synthesized from arachidonic acid. In a small study of 20 MS patients, Gallai *et al*. demonstrated that omega-3 fatty acids actually decreased the serum levels of various proinflammatory cytokines.[36] However, these mechanisms are complex, and the traditional concept that omega-3 fatty acids are anti-inflammatory, and omega-6 fatty acids are proinflammatory, is only partially true, and indeed, obsolete and simplistic.[37,38] In high concentrations, omega-3 fatty acids have anti-coagulatory effects and cause bleeding complications. In western countries, the intake of omega-6 fatty acids is relatively too high when compared with omega-3 fatty acids. The most important sources of omega-3 fatty acids are a number of vegetable oils and sea fish.

### *Omega-6 fatty acids*

Several authors found low levels of linoleic acid in the blood, blood cells and cerebrospinal fluid (CSF) of patients with MS.[39–41] However, the results vary.[42–44] In the brain tissue of MS patients the levels of linoleic acids and other polyunsaturated fatty acids are low.[45] A deficiency in linoleic acid exacerbates the symptoms of the experimental allergic encephalomyelitis (EAE),[46,47] while substitution with linoleic acids acts in a protective fashion.[48,49] In addition to the evidence from the epidemiological studies, these results provided the theoretical basis for clinical studies with linoleic acid.

There have been three randomized intervention studies with linoleic acid (Table 1). All of the studies were relatively small, and the statistical power too small to be able to detect any resultant mild therapeutical effects. Sunflower oil was used as the source of linoleic acid. No study showed any effect on relapse rate and the degree of disability. In two studies, significant differences in the severity and duration of the relapses in favour of active treatment were noted.[50,51] The third study did not show any difference at all between the treatment groups.[52] Thus, these studies do not justify recommending therapy with linoleic acid. However, regarding the pilot character of the study and the small number of patients, the results should not be interpreted as being entirely negative. Possibly, the relative small amount of linoleic acid used in these trials was not the optimum dose, and a larger dose would produce better results.

In a meta-analysis of these trials, Dworkin *et al*. detected significant beneficial effects, more pronounced in the group of patients with mild disability (EDSS 0–2).[53] In the group of severely disabled patients (EDSS 3–6), the positive effects were less consistent, but still visible. Within the mildly disabled patients, the intervention group showed a slower progression of disability ($P = 0.05$) and a better *relapse score* (severity and dura-

**Table 1** Randomized studies with unsaturated fatty acids

| | *Millar, 1973*[51] | *Paty, 1978*[52] | *Bates, 1978*[50] | *Bates, 1989*[61] |
|---|---|---|---|---|
| Patients (*n*) | 75 | 76 | 106 | 292 |
| Therapy | Sunflower oil (17.2 g linoleic acid/day) | Sunflower oil (17 g linoleic acid/day) | Linoleic acid (3 or 23 g/day) | Fish oil (1.7 g EPA, 1.1 g DHA) |
| Placebo | Olive oil (0.4 g linoleic acid/day) | Olive oil (1 g linoleic acid/day) | Oleic acid (4 or 16 g/day) | Olive oil |
| Duration | 24 months | 30 months | 24 months | 24 months |
| Primary outcome | EDSS | EDSS | Number, duration, severity of relapses. Clinical deterioration | EDSS |
| Results | Trend towards fewer relapses and significantly milder relapses with sunflower oil | No difference | No significant difference. Trend in favour of high-dose linoleic acid | No significant difference. Trend in favour of fish oil |

tion) ($P=0.001$). These promising results should justify a larger clinical trial. Unfortunately, this trial has never been undertaken, probably due to the high costs of such a trial and the absence of any commercial interest. Linoleic acid in vegetable oils is readily available in every supermarket and has, therefore, no commercial potential as a pharmaceutical drug whatsoever.

In some countries, evening primrose oil is a popular alternative MS treatment. Evening primrose oil is a vegetable oil rich in gamma linolenic acid, an omega-6 fatty acid.[54] After a randomized study did not show any positive effects,[50] no further studies with evening primrose oil have been undertaken. The dietary needs for omega-6 fatty acids can be satisfied much more easily and cheaply with other vegetable oils.

*Omega-3 fatty acids*

In cardiovascular diseases, there is an increasing body of evidence that omega-3 fatty acids reduce the risk of cardiovascular events and sudden death.[55,56] A large study demonstrated a reduction in cardiovascular mortality from supplementation with omega-3 fatty acids after myocardial infarction.[57] The American Heart Association recommends the intake of omega-3 fatty acids for all patients with coronary heart disease.[55] In various autoimmune diseases, beneficial effects from omega-3 fatty acids are also assumed.[35]

Where MS is concerned, there is not enough data available to be able to confirm the beneficial effect of omega-3 fatty acids. Large controlled studies do not exist. Some investigations found low levels of omega-3 fatty acids in patients with MS.[42,43,58] In contrast to omega-6 fatty acids, in experimental environments, omega-3 fatty acids have not been extensively studied, and the results vary.[34] In the large Nurses' Health Study, there was no association between the incidence of MS and the intake of omega-3 fatty acids from fish.[16]

Nordvik *et al*. treated 16 newly diagnosed patients with omega-3 fatty acids.[59] They observed a reduction in the relapse rate and an improved EDSS. However, this small study was neither randomized nor controlled. Similar results were already published in 1986 in a small sample of 10 patients.[60] Because of the obvious weaknesses of these studies, the results can hardly be used for practical recommendations.

A large, randomized, placebo-controlled study with 292 patients showed no significant differences between active treatment with fish oil (containing high amounts of omega-3 fatty acids) and a placebo (Table 1).[61] However, there were nonsignificant trends in almost all of the results in favour of fish oil. The therapeutic effects were arguably reduced because the patients in the placebo group received dietary advice to increase their intake of polyunsaturated omega-6 fatty acids. From an ongoing randomized study on the effects of a fat-reduced diet with supplementation with omega-3 fatty acids, only provisional data from the first 23 patients is available, suggesting beneficial effects from active treatment.[62]

Today, there is still not enough data available to recommend omega-3 fatty acids for MS. However, due to the generally accepted beneficial effects for cardiovascular diseases, the consumption of sea fish and vegetable oils containing omega-3 fatty acids should be encouraged, independent of the possible effects on MS.

It should also be noted that large amounts of omega-3 fatty acids can create unwanted side effects. High dosages of omega-3 fatty acids (>3 g/day) increase the risk of bleeding complications due to their anti-coagulatory effects. Other side effects include gastrointestinal symptoms, increased LDL-cholesterol levels and hyperglycaemia in patients with diabetes.[55] Therapy with omega-3 fatty acids should, therefore, only be undertaken under medical supervision. The consumption of fish alone will hardly produce concentrations that might lead to unwanted side effects. Irrelevant from the medical point of view, but disappointing and not unproblematic in daily life, is a distinctly fishy smell, which may occur after the intake of large amounts of fish oil.

*Vitamin D*

*Vitamin D: epidemiological evidence and risk of osteoporosis* In MS patients, osteoporosis is a frequent, underdiagnosed and undertreated complication of a chronic vitamin D deficiency which may lead to additional morbidity.[63] The majority of patients suffer from vitamin D deficiency. Nieves *et al*. analysed bone density and laboratory parameters of vitamin D metabolism in women with MS.[64] The bone density and the mean 25(OH) vitamin D levels were much lower compared with a healthy control group. Forty per cent of the patients reported almost no exposure to sunlight.

In a study researching the progression in bone density over two years, the risk of fractures in the absence of major trauma was 10-fold, and the bone loss was seven times greater in MS patients compared with the control group.[65]

In addition, a low intake of vitamin D, immobility, corticosteroid therapy and sun avoidance due to heat sensibility and fatigue makes MS patients prone to osteoporosis.[63,65] Thus, it would seem justifiable to recommend that preventive therapy with vitamin D and calcium should be generally established for MS patients very widely, and in particular for all postmenopausal women and patients receiving repeated corticoid therapy. In everyday practice, this problem is often overlooked: 71% of the postmenopausal women with MS reported by Shabas *et al*. did not take vitamin D, and only 50% used calcium supplements.[63]

*Vitamin D as a specific therapy* A relationship between the geographic distribution of MS, exposure to sunlight, and vitamin D metabolism has been suspected for many years. In northern regions, winter sunlight is not sufficient to produce adequate amounts of vitamin $D_3$. With people who live in regions >42° latitude and have a low intake of vitamin D, a relative vitamin D deficiency during four to six months of the year is common.[66] People who have a particularly high exposure to sunlight suffer from a higher risk of melanoma, but their risk of suffering from MS is reduced.[66,67] Clinical relapses as well as new lesions in

the MRI appear most frequent in spring, when vitamin D storage and 25(OH) vitamin D levels are at their lowest.[68] New lesions in the MRI appear most frequently two months after 25(OH) vitamin D levels were lowest.[69]

Vitamin D exerts numerous immunomodulatory effects.[70] Vitamin D increases the proliferation of lymphocytes and reduces the production of proinflammatory cytokines.[71] In experiments with animals, treatment with vitamin D reduces or prevents the symptoms of EAE.[72,73] The exact mechanisms of this phenomenon have not yet been sufficiently well explained.[70]

A recent prospective epidemiological study supports the hypothesis that vitamin D reduces the incidence of MS. In the US–American Nurses' Health Study, women who took additional vitamin D supplements had a 40% lower risk of MS.[24] However, women who used vitamin D supplements frequently also took other vitamins. This study analysed the association between the intake of vitamin D and the incidence of MS and provides no information on the possible effects of vitamin D in patients already manifesting the disease.

To date, there has not been sufficient evidence to recommend a therapy with vitamin D for MS. Interventional studies with vitamin D are rare. Goldberg *et al.* reported a reduction of the relapse rate after introducing a therapy containing calcium, magnesium and fish liver containing high amounts of Vitamin D.[60] This study was uncontrolled and very small (11 patients). A methodologically better, MR-based pilot study, although equally small, showed no beneficial effects of a therapy with vitamin D.[74]

Patients who wish to perform an experimental therapy with vitamin D should be made aware of the possible side effects of vitamin D. Subsequent to hypercalcaemia, vitamin D may produce cardiac arrhythmias and adynamia. However, the risk of those complications only arises when high amounts of vitamin D ($>1000\,\mu g$/day) are consumed. Most dietary supplements, containing $\leq$ 100 µg vitamin D, are harmless. Renal diseases, sarcoidosis and hypocalcaemia are relative contraindications for vitamin D.

### *Vitamin $B_{12}$*

The link between vitamin $B_{12}$ and MS has been under discussion for more than 50 years.[75] Vitamin $B_{12}$ is a prerequisite for the synthesis of myelin, which has been postulated as an argument for the possible relationship between allegedly low vitamin $B_{12}$ levels and the incidence of MS.[76] Furthermore, vitamin $B_{12}$ deficiency and MS share some clinical and MRI characteristics,[77] indicating common pathophysiological mechanisms.[78] Some authors reported a high prevalence of $B_{12}$ deficiency in patients with MS.[78,79] However, most patients with MS have normal vitamin $B_{12}$ levels.[80] Nijst *et al.* found low vitamin $B_{12}$ concentrations in the CSF of MS patients, while the serum levels were within normal limits.[81] In addition to inadequate dietary intake, gastrointestinal malabsorption is not uncommon in MS and may contribute to vitamin $B_{12}$ deficiency.[82] Immediately after corticoid treatment, the concentrations of folic acid and vitamin $B_{12}$ are decreased.[83] It is also possible that many patients do not have an absolute vitamin $B_{12}$ deficiency, but suffer from a disturbance in the metabolism of vitamin $B_{12}$.[78]

Controlled, large intervention studies with vitamin $B_{12}$ do not exist. A high dosage therapy with vitamin $B_{12}$ over six months in six severely disabled patients showed no clinical benefit. However, a reduction in the latency of the potentials noted during the course of the study was interpreted as an indication of the effectiveness of the therapy.[84] In a placebo-controlled trial with 138 patients, Wade *et al.* found small, but insignificant, beneficial effects from a high-dosage therapy of parenteral vitamin $B_{12}$ (combined with lofepramine and l-phenylalanine, the 'Cari Loder Regime').[85]

Currently, there is no scientific basis to recommend supplementing the diet with vitamin $B_{12}$ apart from in the treatment of vitamin deficiencies. Vitamin $B_{12}$ deficiency in MS patients is not unusual. Therefore, these patients should be meticulously screened, in particular, as the typical neurological signs of vitamin $B_{12}$ deficiency may be imitated or aggravated by MS symptoms.[77]

### *Selenium*

Oxidative stress possibly plays a key role in the pathophysiology of MS.[86] Therefore, because of its potent antioxidant properties, selenium may have a positive effect on the course of the disease. There is no reliable data available as to how many patients use selenium but our own experience suggests that a large proportion of MS patients use dietary supplements containing selenium, often combined with vitamins C and E, which also produce antioxidant effects. It is frequently claimed that selenium deficiency is both a common and important problem in MS. Indeed, clinical studies have yielded mixed results. In Finnish patients, the selenium content in the blood was markedly lower than in healthy control groups.[87] Clausen *et al.* found low selenium levels and lowered glutathione peroxidase activities in the erythrocytes of MS patients.[88] However, in a previous study some years earlier, the same authors described normal blood selenium levels. Compared with healthy control groups, the selenium concentrations in the erythrocytes of MS patients were even higher.[89] Other authors also found higher or comparable selenium levels in the blood and erythrocytes of MS patients.[31,90] The conclusion arrived at was that the decreased glutathione peroxidase activity found in the erythrocytes of MS patients,[88,91] a surrogate marker of antioxidant capacity, is irrespective of the selenium levels, and is primarily the result of genetic factors.[31]

An intervention study with selenium and vitamins C and E increased the activity of glutathione peroxidase in various blood cells of the patients treated.[92] However, no beneficial clinical effects were determined.

An important aspect of every therapy with antioxidants is the question as to whether the substances are capable of passing the blood–brain barrier. In the presence of an intact blood–brain barrier, most antioxidants do not penetrate it.[93] Analyses of selenium levels in whole blood or erythrocytes are, for that reason, of questionable relevance.

### *Other antioxidant vitamins and compounds*

A study with 36 patients showed low levels of vitamin E in serum and CSF, but there was no association with clinical variables.[94] A recent large epidemiological trial yielded no correlation between the intake of the antioxidants vitamin C, carotinoids and vitamin E and the incidence of MS.[95] This study confirms several previous case-control studies which also found no correlation between the risk of MS and the intake of fruit and vegetables rich in vitamins A, C and E.[12,14] These vitamins are harmless if their intake does not exceed the recommended maximum doses. Vitamin A should not be taken by women during pregnancy. There are no results available from clinical studies suggesting beneficial effects from vitamins A, C and E in MS.

In addition to vitamins, a large number of antioxidant compounds such as coenzyme Q10, alpha-lipoic acid and anthocyanes from red wine or grape extracts are taken by MS patients. It is indisputable that these substances act as antioxidants. However, their effects on MS are entirely speculative. Some antioxidants have immunostimulatory effects which, theoretically, could also generate negative effects in MS.[96] The consumption of antioxidants should be discouraged until valid clinical data on the safety and efficacy of these substances is available.

### *Other minerals*

The role of calcium has been discussed above. Zinc deficiency may predispose patients to pressure sores.[30] There is not enough data on iron or magnesium supplements, which are frequently taken by MS patients, to be able to draw valid conclusions.

### *The Swank diet*

Worldwide, a large number of differing special diets for MS are propagated and followed by many patients. No clinical benefit from any of these diets has been proven. For most of these diets there is no scientific data available at all, and some of them are quite bizarre, based on dubious or plainly wrong pathophysiological considerations. The Swank diet is one example of the more popular diets based on pathophysiological considerations.

Using studies in Scandinavia which suggested a link between intake of saturated fatty acids and the incidence of MS as his argument,[6] Swank developed a special diet for MS patients. The main aim of the Swank diet is a drastic reduction in saturated fat.[97] No more than 15 g/day saturated fat is to be consumed, which means a radical change in the usual dietary habits in the USA and Europe. Fatty dairy products ( $>1\%$ fat) are not allowed. Frequent seafood meals are recommended. In addition to the reduced fat intake, 15 g/day vegetable oil and 5 g/day cod liver oil are consumed (a source of omega-3 fatty acids and vitamin D). In contrast to other inventors of MS diets, Swank wished to provide his dietary therapy with a scientific justification and monitored the patients for many years.[98,99] One hundred and forty-four MS patients adhering to the Swank diet were observed over 34 years.[99]

Those patients who followed the dietary instructions strictly had a slower progression of disability and lower mortality than patients who ingested more than 20 g/day fat. The effects were most pronounced in patients who were only moderately disabled when treatment began. After commencing the diet, the relapse rate declined markedly (prior to the diet one relapse/year, after five years of diet 0.1 relapse/year). At first sight, these results look very promising. However, the validity of the study is limited, because it was neither controlled nor blinded or randomized. It can be assumed that there was a considerable selection bias, as patients who perceive no benefit from a particular therapy are not very likely to continue over a period of 34 years. Because of these methodological problems, the possible benefits from the Swank diet can by no means be judged as proven. However, it can be assumed that strict adherence to the Swank diet will reduce cardiovascular mortality.

### *Summary and recommendations*

MS is not a metabolic disorder. No beneficial effects from any particular diet have been proven. Therefore, the same recommendations concerning a well balanced diet apply equally as they do for the population in general. Malnutrition, vitamin deficiencies, obesity and weight loss are common and may exacerbate the clinical symptoms. There is no basis for recommendations to avoid particular foods (e.g., alcohol, meat, wheat/gluten, coffee, animal fat). Some dietary therapies, particularly those that exclude whole food groups, are potentially harmful as they can lead to malnutrition. In certain situations (constipation, fatigue, dysphagia, etc.) a modification of the nutritional habits may lead to an improvement in the clinical symptoms.

Epidemiological studies indicate a correlation between the consumption of animal fat and the incidence of MS. Moreover, there are abundant findings from experiments on animals and theoretical considerations to suggest beneficial effects from unsaturated fatty acids. A meta-analysis of three controlled trials suggested a clinical benefit from linoleic acid. Although there is as yet no definite proof for this recommendation, it would seem justifiable to satisfy the need for fat predominantly with high-quality vegetable oils with a high content of unsaturated fatty acids, and to take two or more seafood meals

per week. It remains a subject of speculation whether supplementing with various minerals, trace elements, fish oil or vitamins is helpful. One exception is the prophylaxis of osteoporosis with calcium and vitamin D, which should be widely recommended. Diets that forbid dairy foods can provoke vitamin D deficiency and could consequently be harmful. Dietary supplements with no proof of their efficacy, which are freely available, should be viewed with great caution. However, in our experience it is frequently not helpful to actively discourage a patient from a certain diet or other alternative therapy if she or he strongly believes in its efficacy even if this is highly questionable or very improbable from a medical point of view. Usually, these therapies are quite harmless, although frequently quite expensive.

The possible relationships between MS and nutrition have not been adequately researched. There is not enough clinical trial data or reliable information available to advocate the use of any particular diet or dietary supplement as a disease-modifying therapy. However, it seems probable that, in the future, a modification in diet or dietary supplements might be recommended as a treatment for MS.

## References

1 Winterholler M, Erbguth F, Neundörfer B. Verwendung paramedizinischer Verfahren durch MS-Patienten-Patientencharakterisierung und Anwendungsgewohnheiten. *Fortschr Neurol Psychiatr* 1997; **65**: 555–61.
2 Schwartz CE, Laitin E, Brotman S, LaRocca N. Utilization of unconventional treatments by persons with MS: is it alternative or complementary? *Neurology* 1999; **52**: 626–29.
3 Alter M, Yamoor M, Harshe M. Multiple sclerosis and nutrition. *Arch Neurol* 1974; **31**: 267–72.
4 Coo H, Aronson KJ. A systematic review of several potential non-genetic risk factors for multiple sclerosis. *Neuroepidemiology* 2004; **23**: 1–12.
5 Lauer K. Diet and multiple sclerosis. *Neurology* 1997; **49**: S55–61.
6 Swank RL, Lerstad O, Strom P, Barker J. Multiple sclerosis in rural Norway; its geographic and occupational incidence in relation to nutrition. *N Engl J Med* 1952; **246**: 721–28.
7 Agranoff BW, Goldberg D. Diet and the geographical distribution of multiple sclerosis. *Lancet* 1974; **2**: 1061–66.
8 Knox EG. Foods and diseases. *Br J Prev Soc Med* 1977; **31**: 71–80.
9 Butcher J. The distribution of multiple sclerosis in relation to the dairy industry and milk consumption. *N Z Med J* 1976; **83**: 427–30.
10 Lauer K. The risk of multiple sclerosis in the USA in relation to sociogeographic features: a factor-analytic study. *J Clin Epidemiol* 1994; **47**: 43–48.
11 Esparza ML, Sasaki S, Kesteloot H. Nutrition, latitude, and multiple sclerosis mortality: an ecologic study. *Am J Epidemiol* 1995; **142**: 733–37.
12 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.
13 Cendrowski W, Wender M, Dominik W, Flejsierowicz Z, Owsianowski M, Popiel M. Epidemiological study of multiple sclerosis in western Poland. *Eur Neurol* 1969; **2**: 90–108.
14 Berr C, Puel J, Clanet M, Ruidavets JB, Mas JL, Alperovitch A. Risk factors in multiple sclerosis: a population-based case-control study in Hautes-Pyrenees, France. *Acta Neurol Scand* 1989; **80**: 46–50.
15 Tola MR, Granieri E, Malagu S, Caniatti L, Casetta I, Govoni V *et al*. Dietary habits and multiple sclerosis. A retrospective study in Ferrara, Italy. *Acta Neurol (Napoli)* 1994; **16**: 189–97.
16 Zhang SM, Willett WC, Hernan MA, Olek MJ, Ascherio A. Dietary fat in relation to risk of multiple sclerosis among two large cohorts of women. *Am J Epidemiol* 2000; **152**: 1056–64.
17 Sepcic J, Mesaros E, Materljan E, Sepic-Grahovac D. Nutritional factors and multiple sclerosis in Gorski Kotar, Croatia. *Neuroepidemiology* 1993; **12**: 234–40.
18 Murrell TG, Matthews BJ. Multiple sclerosis – one manifestation of neurobrucellosis? *Med Hypotheses* 1990; **33**: 43–48.
19 Ghadirian P, Jain M, Ducic S, Shatenstein B, Morisset R. Nutritional factors in the aetiology of multiple sclerosis: a case-control study in Montreal, Canada. *Int J Epidemiol* 1998; **27**: 845–52.
20 Poskanzer DC, Sheridan JL, Prenney LB, Walker AM. Multiple sclerosis in the Orkney and Shetland Islands. II: The search for an exogenous aetiology. *J Epidemiol Community Health* 1980; **34**: 240–52.
21 Lauer K. Multiple sclerosis in relation to meat preservation in France and Switzerland. *Neuroepidemiology* 1989; **8**: 308–15.
22 Pisacane A, Impagliazzo N, Russo M, Valiani R, Mandarini A, Florio C *et al*. Breast feeding and multiple sclerosis. *BMJ* 1994; **308**: 1411–12.
23 Spencely M, Dick G. Breast feeding and multiple sclerosis. *Neuroepidemiology* 1982; **1**: 216–22.
24 Munger KL, Zhang SM, O'Reilly E, Hernan MA, Olek MJ, Willett WC *et al*. Vitamin D intake and incidence of multiple sclerosis. *Neurology* 2004; **62**: 60–65.
25 Thomas FJ, Wiles CM. Dysphagia and nutritional status in multiple sclerosis. *J Neurol* 1999; **246**: 677–82.
26 Slawta JN, Wilcox AR, McCubbin JA, Nalle DJ, Fox SD, Anderson G. Health behaviors, body composition, and coronary heart disease risk in women with multiple sclerosis. *Arch Phys Med Rehabil* 2003; **84**: 1823–30.
27 Hewson DC, Phillips MA, Simpson KE, Drury P, Crawford MA. Food intake in multiple sclerosis. *Hum Nutr Appl Nutr* 1984; **38**: 355–67.
28 Timmerman GM, Stuifbergen AK. Eating patterns in women with multiple sclerosis. *J Neurosci Nurs* 1999; **31**: 152–58.
29 Payne A. Nutrition and diet in the clinical management of multiple sclerosis. *J Hum Nutr Diet* 2001; **14**: 349–57.
30 Williams CM, Lines CM, McKay EC. Iron and zinc status in multiple sclerosis patients with pressure sores. *Eur J Clin Nutr* 1988; **42**: 321–28.
31 Smith DK, Feldman EB, Feldman DS. Trace element status in multiple sclerosis. *Am J Clin Nutr* 1989; **50**: 136–40.
32 Cook AW, Gupta JK, Pertschuk LP, Nidzgorski F. Multiple sclerosis and malabsorption. *Lancet* 1978; **i**: 1366.
33 White R, Ashworth A. How drug therapy can affect, threaten and compromise nutritional status. *J Hum Nutr Diet* 2000; **13**: 119–29.
34 Harbige LS. Dietary n-6 and n-3 fatty acids in immunity and autoimmune disease. *Proc Nutr Soc* 1998; **57**: 555–62.
35 Simopoulos AP. Omega-3 fatty acids in inflammation and autoimmune diseases. *J Am Coll Nutr* 2002; **21**: 495–505.
36 Gallai V, Sarchielli P, Trequattrini A, Franceschini M, Floridi A, Firenze C *et al*. Cytokine secretion and eicosanoid production in the peripheral blood mononuclear cells of MS patients undergoing dietary supplementation with n-3 polyunsaturated fatty acids. *J Neuroimmunol* 1995; **56**: 143–53.

37 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.
38 Calder PC. Polyunsaturated fatty acids, inflammation, and immunity. *Lipids* 2001; **36**: 1007–24.
39 Neu IS. Essential fatty acids in the serum and cerebrospinal fluid of multiple sclerosis patients. *Acta Neurol Scand* 1983; **67**: 151–63.
40 Navarro X, Segura R. Plasma lipids and their fatty acid composition in multiple sclerosis. *Acta Neurol Scand* 1988; **78**: 152–57.
41 Fisher M, Johnson MH, Natale AM, Levine PH. Linoleic acid levels in white blood cells, platelets, and serum of multiple sclerosis patients. *Acta Neurol Scand* 1987; **76**: 241–45.
42 Nightingale S, Woo E, Smith AD, French JM, Gale MM, Sinclair HM *et al*. Red blood cell and adipose tissue fatty acids in mild inactive multiple sclerosis. *Acta Neurol Scand* 1990; **82**: 43–50.
43 Holman RT, Johnson SB, Kokmen E. Deficiencies of polyunsaturated fatty acids and replacement by nonessential fatty acids in plasma lipids in multiple sclerosis. *Proc Natl Acad Sci* 1989; **86**: 4720–24.
44 Yoshida M, Takase S, Itahara K, Nakanishi T. Linoleate and fatty acid compositions in the serum lipids of Japanese patients with multiple sclerosis. *Acta Neurol Scand* 1983; **68**: 362–64.
45 Alling C, Vanier MT, Svennerholm L. Lipid alterations in apparently normal white matter in multiple sclerosis. *Brain Res* 1971; **35**: 325–36.
46 Clausen J, Moller J. Allergic encephalomyelitis induced by brain antigen after deficiency in polyunsaturated fatty acids during myelination. Is multiple sclerosis a nutritive disorder? *Acta Neurol Scand* 1967; **43**: 375–88.
47 Clausen J, Moller J. Experimental allergic encephalomyelitis provoked in rats after developmental lack of polyunsaturated tally acids. *Acta Neurol Scand* 1967; **43**: 74.
48 Meade CJ, Mertin J, Sheena J, Hunt R. Reduction by linoleic acid of the severity of experimental allergic encephalomyelitis in the guinea pig. *J Neurol Sci* 1978; **35**: 291–308.
49 Harbige LS, Layward L, Morris-Downes MM, Dumonde DC, Amor S. The protective effects of omega-6 fatty acids in experimental autoimmune encephalomyelitis (EAE) in relation to transforming growth factor-beta 1 (TGF-beta1) upregulation and increased prostaglandin E2 (PGE2) production. *Clin Exp Immunol* 2000; **122**: 445–52.
50 Bates D, Fawcett PR, Shaw DA, Weightman D. Polyunsaturated fatty acids in treatment of acute remitting multiple sclerosis. *Br Med J* 1978; **2**: 1390–91.
51 Millar JH, Zilkha KJ, Langman MJ, Wright HP, Smith AD, Belin J *et al*. Double-blind trial of linoleate supplementation of the diet in multiple sclerosis. *Br Med J* 1973; **1**: 765–68.
52 Paty DW, Cousin HK, Read S, Adlakha K. Linoleic acid in multiple sclerosis: failure to show any therapeutic benefit. *Acta Neurol Scand* 1978; **58**: 53–58.
53 Dworkin RH, Bates D, Millar JH, Paty DW. Linoleic acid and multiple sclerosis: a reanalysis of three double-blind trials. *Neurology* 1984; **34**: 1441–45.
54 Gibson RA, Lines DR, Neumann MA. Gamma linolenic acid (GLA) content of encapsulated evening primrose oil products. *Lipids* 1992; **27**: 82–84.
55 Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation* 2002; **106**: 2747–57.
56 Albert CM, Campos H, Stampfer MJ, Ridker PM, Manson JE, Willett WC *et al*. Blood levels of long-chain n-3 fatty acids and the risk of sudden death. *N Engl J Med* 2002; **346**: 1113–18.
57 Marchioli R, Barzi F, Bomba E, Chieffo C, Di Gregorio D, Di Mascio R *et al*. Early protection against sudden death by n-3 polyunsaturated fatty acids after myocardial infarction: time-course analysis of the results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI)-Prevenzione. *Circulation* 2002; **105**: 1897–903.
58 Cunnane SC, Ho SY, Dore-Duffy P, Ells KR, Horrobin DF. Essential fatty acid and lipid profiles in plasma and erythrocytes in patients with multiple sclerosis. *Am J Clin Nutr* 1989; **50**: 801–806.
59 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**: 143–49.
60 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.
61 Bates D, Cartlidge NE, French JM, Jackson MJ, Nightingale S, Shaw DA *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.
62 Weinstock-Guttmann B, Baier M, LeeKwen P, Feichter J, Dinehart S, Venkatraman J *et al*. A randomized study of low-fat diet with omega-3 fatty acid supplementation in patients with relapsing–remitting multiple sclerosis (RRMS). *Neurology* 2002; **58**: A461–62.
63 Shabas D, Weinreb H. Preventive healthcare in women with multiple sclerosis. *J Womens Health Gend Based Med* 2000; **9**: 389–95.
64 Nieves J, Cosman F, Herbert J, Shen V, Lindsay R. High prevalence of vitamin D deficiency and reduced bone mass in multiple sclerosis. *Neurology* 1994; **44**: 1687–92.
65 Cosman F, Nieves J, Komar L, Ferrer G, Herbert J, Formica C *et al*. Fracture history and bone loss in patients with MS. *Neurology* 1998; **51**: 1161–65.
66 Webb AR, Kline L, Holick MF. Influence of season and latitude on the cutaneous synthesis of vitamin D3: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D3 synthesis in human skin. *J Clin Endocrinol Metab* 1988; **67**: 373–78.
67 Freedman DM, Dosemeci M, Alavanja MC. Mortality from multiple sclerosis and exposure to residential and occupational solar radiation: a case-control study based on death certificates. *Occup Environ Med* 2000; **57**: 418–21.
68 Hayes CE. Vitamin D: a natural inhibitor of multiple sclerosis. *Proc Nutr Soc* 2000; **59**: 531–35.
69 Embry AF, Snowdon LR, Vieth R. Vitamin D and seasonal fluctuations of gadolinium-enhancing magnetic resonance imaging lesions in multiple sclerosis. *Ann Neurol* 2000; **48**: 271–72.
70 Hayes CE, Nashold FE, Spach KM, Pedersen LB. The immunological functions of the vitamin D endocrine system. *Cell Mol Biol* 2003; **49**: 277–300.
71 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**: 135–38.
72 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**: 7861–64.
73 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**: 171–79.

74 Fleming JO, Hummel AL, Beinlich BR, Borowski BJ, Peebles T, Colburn M *et al*. Vitamin D treatment of relapsing–remitting multiple sclerosis (RRMS): a MRI-based pilot study. *Neurology* 2000; **54**: A338.
75 Simson G, Herfort A, Krim M, Meyer LM. Effects of vitamin B12 in multiple sclerosis. *Proc Soc Exp Biol Med* 1950; **75**: 721.
76 Sandyk R, Awerbuch GI. Vitamin B12 and its relationship to age of onset of multiple sclerosis. *Int J Neurosci* 1993; **71**: 93–99.
77 Ghezzi A, Zaffaroni M. Neurological manifestations of gastrointestinal disorders, with particular reference to the differential diagnosis of multiple sclerosis. *Neurol Sci* 2001; **22**: S117–22.
78 Reynolds EH. Multiple sclerosis and vitamin B12 metabolism. *J Neuroimmunol* 1992; **40**: 225–30.
79 Simpson CA. Vitamin B12 levels in the serum and cerebrospinal fluid in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1964; **27**: 174–77.
80 Goodkin DE, Jacobsen DW, Galvez N, Daughtry M, Secic M, Green R. Serum cobalamin deficiency is uncommon in multiple sclerosis. *Arch Neurol* 1994; **51**: 1110–14.
81 Nijst TQ, Wevers RA, Schoonderwaldt HC, Hommes OR, de Haan AF. Vitamin B12 and folate concentrations in serum and cerebrospinal fluid of neurological patients with special reference to multiple sclerosis and dementia. *J Neurol Neurosurg Psychiatry* 1990; **53**: 951–54.
82 Gupta JK, Ingegno AP, Cook AW, Pertschuk LP. Multiple sclerosis and malabsorption. *Am J Gastroenterol* 1977; **68**: 560–65.
83 Frequin ST, Wevers RA, Braam M, Barkhof F, Hommes OR. Decreased vitamin B12 and folate levels in cerebrospinal fluid and serum of multiple sclerosis patients after high-dose intravenous methylprednisolone. *J Neurol* 1993; **240**: 305–308.
84 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**: 82–86.
85 Wade DT, Young CA, Chaudhuri KR, Davidson DL. A randomised placebo controlled exploratory study of vitamin B-12, lofepramine, and L-phenylalanine (the 'Cari Loder regime') in the treatment of multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2002; **73**: 246–49.
86 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**: 261–68.
87 Wikstrom J, Westermarck T, Palo J. Selenium, vitamin E and copper in multiple sclerosis. *Acta Neurol Scand* 1976; **54**: 287–90.
88 Clausen J, Jensen GE, Nielsen SA. Selenium in chronic neurologic diseases. Multiple sclerosis and Batten's disease. *Biol Trace Elem Res* 1988; **15**: 179–203.
89 Jensen GE, Gissel-Nielsen G, Clausen J. Leucocyte glutathione peroxidase activity and selenium level in multiple sclerosis. *J Neurol Sci* 1980; **48**: 61–67.
90 Mazzella GL, Sinforiani E, Savoldi F, Allegrini M, Lanzola E, Scelsi R. Blood cells glutathione peroxidase activity and selenium in multiple sclerosis. *Eur Neurol* 1983; **22**: 442–46.
91 Szeinberg A, Golan R, Ben-Ezzer J, Sarova-Pinhas I, Kindler D. Glutathione peroxidase activity in various types of blood cells in multiple sclerosis. *Acta Neurol Scand* 1981; **63**: 67–75.
92 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**: S450–53.
93 Gilgun-Sherki Y, Melamed E, Offen D. Oxidative stress-induced neurodegenerative diseases: the need for antioxidants that penetrate the blood brain barrier. *Neuropharmacology* 2001; **40**: 959–75.
94 Jimenez-Jimenez FJ, de Bustos F, Molina JA, de Andres C, Gasalla T, Orti-Pareja M *et al*. Cerebrospinal fluid levels of alpha-tocopherol in patients with multiple sclerosis. *Neurosci Lett* 1998; **249**: 65–67.
95 Zhang SM, Hernan MA, Olek MJ, Spiegelman D, Willett WC, Ascherio A. Intakes of carotenoids, vitamin C, and vitamin E and MS risk among two large cohorts of women. *Neurology* 2001; **57**: 75–80.
96 Bowling AC, Stewart TM. Current complementary and alternative therapies for multiple sclerosis. *Curr Treat Options Neurol* 2003; **5**: 55–68.
97 Swank RL. Treatment of multiple sclerosis with a low-fat diet. *J Am Diet Assoc* 1960; **36**: 322–25.
98 Swank RL. Multiple sclerosis: twenty years on low fat diet. *Arch Neurol* 1970; **23**: 460–74.
99 Swank RL, Dugan BB. Effect of low saturated fat diet in early and late cases of multiple sclerosis. *Lancet* 1990; **336**: 37–39.