

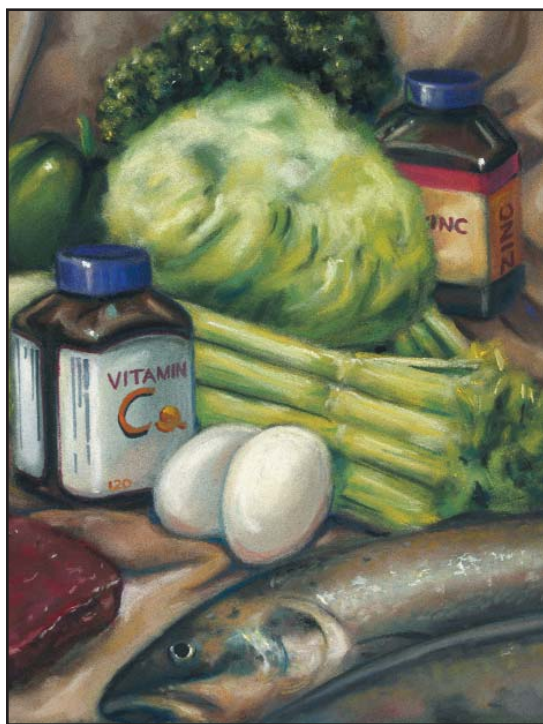
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# Nutritional Management of Multiple Sclerosis

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## INTRODUCTION

Multiple Sclerosis (MS) is an autoimmune neurological disease associated with inflammation of the myelin sheaths of the central and peripheral nervous systems (CNS and PNS respectively).<sup>1,2,3</sup> The normal function of myelin is to provide an insulation barrier essential for propagation of neuronal impulses. Since demyelination and impaired neuronal transmission are the hallmarks of the disease, patients diagnosed with MS often present with deficits in vision, strength, sensation and/or coordination.

MS mainly affects young adults, with peak incidence at age 30. Although the incidence in women is higher than in men (3:2 ratio), men tend to experience a more debilitating form of the disease. Additionally, MS is twice as likely to occur in Caucasians than Blacks, while the disease is rarely reported in populations of oriental origin.<sup>4,5</sup> Of the various types of MS, relapsing-remitting MS (RRMS) affects approximately 85% of

all patients.<sup>5</sup> Patients diagnosed with RRMS display a characteristic cyclical pattern of the disease characterized by periods of remission, followed by intervals of relapses that present as an acute 'flare-up' or 'exacerbation'. The course of RRMS varies greatly between individuals, however up to 75% of these patients can progress to the secondary progressive form of the disease (SPMS). SPMS is a more debilitating form of the disease defined by a gradual, continuous decline in neurological function, with or without further relapses.<sup>6</sup>

SOME DISEASE-RELATED SYMPTOMS INCLUDE WEAKNESS, NUMBNESS, FATIGUE, TREMOR, MUSCLE SPASMS, PAIN, DIZZINESS, URINARY INCONTINENCE, AND COGNITIVE IMPAIRMENT.

The treatment goal in RRMS patients is to increase the duration of remissions and reduce the number and severity of relapses. Analogous to the goals of drug therapy, the goal of nutritional intervention is to improve patients' quality of life by reducing the severity of the numerous disease-induced symptoms. As a result, the combination of appropriate drug therapy and nutritional intervention maximizes symptom management.

Some disease-related symptoms include weakness, numbness, fatigue, tremor, muscle spasms, pain, dizziness, urinary incontinence, and cognitive impairment. During the course of MS, secondary conditions such as bowel problems, decreased ambulation, pressure sores, dysphagia, and reduced appetite also occur. These disease-induced symptoms can affect patients' nutritional status and ultimately their quality of life. Evidence has shown that optimal nutrition can reduce the risk of developing secondary conditions associated with MS, decrease the risk of developing other chronic diseases and enhance overall quality of life.<sup>4,7-9</sup> In addition to symptom management, it has been suggested that a correlation between nutritional intake and geographical location influences the risk of patients acquiring MS.<sup>3,10,11</sup> Optimal nutritional management is an integral component in holistic patient care that directly impacts on many disease-induced symptoms.

## NUTRITIONAL MANAGEMENT

Since the cure for MS remains elusive, patients willingly seek alternative methods that may alleviate symptoms or delay disease progression. Unfortunately, patient decisions are not always based on sound nutritional recommendations. As a result,

macronutrient and micronutrient deficiencies can develop, thereby placing patients at risk of adverse secondary conditions or malnutrition. Conversely, dietary supplementation with exceedingly high doses of macronutrients or vitamins and minerals is not only a risk for toxicity, but can also lead to deficiencies due to competitive binding to enzymes and transport proteins. Although complementary and alternative therapies have gained popularity over the years, careful consideration is required to ensure safety and efficacy.

## MACRONUTRIENTS

The body requires three macronutrients (fat, carbohydrate, and protein) to fuel its metabolic and physical activities. Nervous tissue contains large amounts of lipids, therefore particular attention has been directed to the role of dietary fat and their possible therapeutic effects in patients with MS.<sup>3,12</sup> Dietary lipids provide a concentrated source of energy, transport fat-soluble vitamins and are a source of essential fatty acids.

### Fatty Acids

The physical properties that distinguish fatty acids are the number of carbon double bonds in the hydrocarbon chain. Saturated fatty acids (SFA) do not contain double bonds, are solid at room temperature, and are present in meat, butterfat and in coconut and palm kernel oils. Monounsaturated fatty acids (MUFA) contain one double bond and are present in canola, olive and peanut oils, and in soft margarine. According to the American Heart Association (AHA), SFA should be limited to 7–10% of total calories per day, and MUFA should comprise up to 10% of total calories. Recommendations

for fat intake for individuals with MS suggest 30% of energy should be provided as fat, although saturated fat should be restricted to less than 20 g per day.<sup>2,13</sup> Thus, in a patient with a dietary intake of 1800 calories/day, the AHA's recommendation of 7 to 10% saturated fat would translate into 14 to 20 g of saturated fat per day and would fall within the recommended limit (<20 g/day).

### Saturated Fatty Acids

Since the early 1950's, it has been proposed that high consumption of saturated fat, particularly from animal fat, butterfat, shortening, and hydrogenated oils may be involved in the etiology and course of MS. Since lipids are the main component of the myelin sheath, excess SFA are thought to alter the stability of the myelin sheath, thereby resulting in an increased susceptibility to demyelination.<sup>11,14,15</sup> Findings from numerous studies appear to be consistent, suggesting that lower consumption of saturated fat (i.e. <20 g/day) is related to significantly fewer exacerbations, slower deterioration, and lower death rates. Patients consuming 10–15 g per day or less of saturated fat had improved energy levels and less fatigue.<sup>5,10,14,16-22</sup> On the other hand, saturated fat intake of approximately 20–42 g per day was associated with increased disability and three times the death rate. As a result, MS patients who adopt a diet low in saturated fat, are likely to show improvements in energy and fatigue profiles.<sup>14</sup>

### Polyunsaturated Fatty Acids

Approximately one-third of nervous tissue consists of polyunsaturated fatty acids (PUFA). PUFA are described as linoleic acid, or omega-6 fatty acid (n-6), and alpha-linolenic acid, or omega-3 fatty acid (n-3).

Their designation is based on the location of the double bond in the hydrocarbon chain. Despite the fact that n-6 and n-3 fatty acids are considered to be essential, the body cannot synthesize them, therefore they must be obtained in the diet.<sup>23-25</sup> n-6 fatty acids are derived from vegetable oils, result in the production of arachidonic acid (AA), and are present in cell membranes (see Figure 1). In contrast, n-3 fatty acids are required for the production of eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA), which are also found in ocean fish, fish oil and cod liver oil.<sup>2,26,27</sup> AA and DHA are major components of membrane phospholipids, including those in the brain and retina, and are involved in maintaining the structure and integrity of cell membranes, cell membrane lipid synthesis, and signal transduction mechanisms. AA and EPA are precursors of eicosanoids, otherwise known as hormone-like compounds, that are fundamental for prostaglandin (PG) and leukotriene production, and for regulating blood pressure, heart rate, immune and inflammatory responses.<sup>28,29</sup>

In the event of acute tissue injury, PGE<sub>2</sub> serves as an initial mediator of inflammation. Chronically, PGE<sub>2</sub> exerts an immunosuppressive action via increased proliferation of suppressor T-cells and decreased migration of helper T-cells.<sup>30-32</sup>

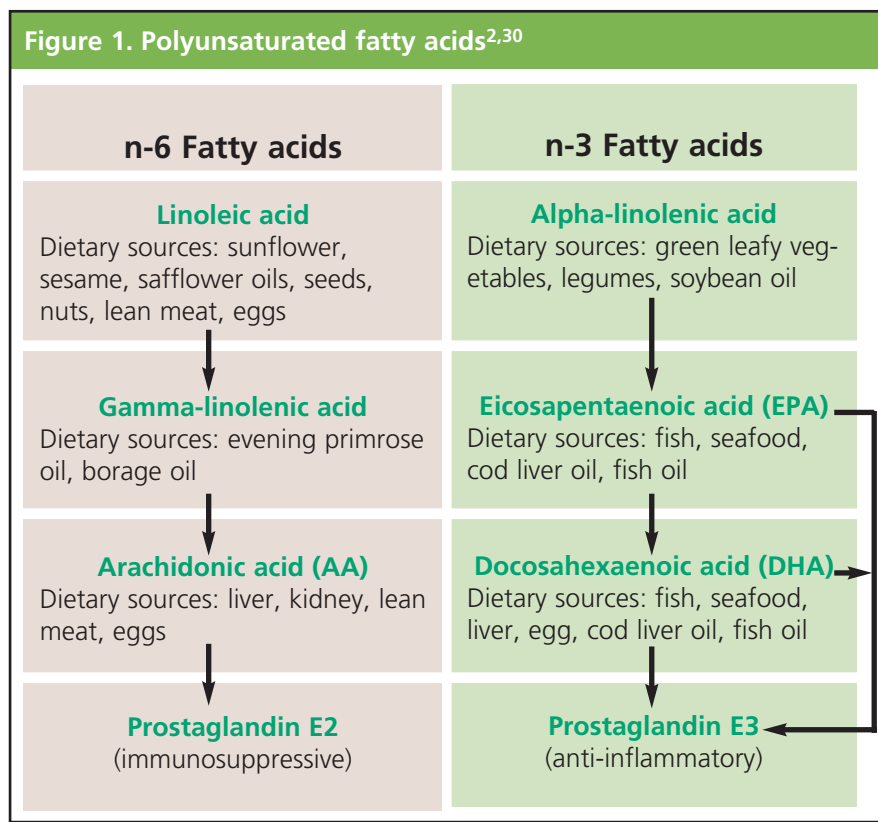
It has been suggested that the immunosuppressive effect of elevated levels of PGE<sub>2</sub>, resulting from the synthesis of AA may benefit patients with MS.<sup>33</sup> In controlled studies, supplementing the diet with 20-25 g of n-6 fatty acids has produced favourable effects on the severity of relapses and on the progress of disability in early cases

of MS. Long-term effects on the course of the disease were not evident with n-6 supplementation.<sup>33-35</sup>

As previously stated, MS is associated with inflammation. The synthesis of EPA results in the production of PGE<sub>3</sub>, which exerts an anti-inflammatory response.<sup>11,30,36</sup> Interestingly, patients with MS have lower plasma concentrations of n-3 fatty acids. In a multicentre, double-blind, controlled study, 312 patients were allocated to two groups. Both groups were advised by a dietitian to reduce animal fat intake and increase intake of n-6 PUFA. Diets of the treatment group were supplemented with n-3 PUFA. Adequate intake of n-6 fatty acids was required to ensure the immunosuppressive effects of n-6 fatty acids outweighed the immune-enhancing

effects of chronic n-3 supplementation while maximizing the known anti-inflammatory effects of n-3 fatty acids. There was a significant increase in serum EPA and DHA (n-3 fatty acids) in patients receiving n-3 supplements. Assessment of the frequency, duration and severity of relapses favoured the treatment group, however the results were not statistically significant.<sup>37</sup>

In a recent uncontrolled study, the diets of sixteen consecutive, newly-diagnosed patients with MS were supplemented with fish oil and vitamins. The patients received nutritional advice, including a recommendation to reduce saturated fat intake and increase fish consumption. After two years of follow-up there was a significant increase in plasma phospholipid concentrations



## MS PATIENTS ON NSAID THERAPY MUST BE CLOSELY MONITORED TO ENSURE THAT DISEASE-INDUCED DETERIORATION DOES NOT OCCUR.

of n-3 fatty acids, and a decrease in all n-6 fatty acids with the exception of AA. Although the sample size was small, the dietary changes were associated with a significant reduction in the mean and annual exacerbation rates and mean Expanded Disability Status Scale scores.<sup>11</sup> The benefits of n-3 supplementation have also been demonstrated in other inflammatory autoimmune diseases.<sup>25,38</sup>

Despite the above stated benefits of n-3 supplementation, the overall advantage of n-3 compared to n-6 supplementation is controversial. It is well known that n-6 and n-3 metabolic pathways compete for the same rate-limiting enzyme (delta-6 desaturase), however the enzyme favours the n-3 pathway over the n-6 pathway.<sup>39</sup> In a recent study, rats were fed formula supplemented with DHA (n-3 fatty acid) resulting in higher levels of DHA and lower levels of AA (n-6 fatty acid) in the brain and red blood cells.<sup>40</sup> Ultimately, this can reduce the distribution of these compounds into cell membranes and possibly alter the synthesis of eicosanoids responsible for immunosuppressive action driven by the production of PGE2. Conversely, rats supplemented with AA had higher levels of AA and lower levels of DHA in red blood cells and brain tissue, which could have potentially affected leukotriene and prostaglandin formation required for the PGE3-mediated anti-inflammatory response.<sup>11,40</sup> These studies demonstrate that a balance of n-3 and n-6 intake may be more important than the total or absolute amount of each fatty acid. Current nutritional recommendations for PUFA are 20–25 g per day, which is equivalent to approximately 10% of the total calories proposed by the AHA. It has also been suggested that at least 20 g per day of PUFA be n-6 fatty acids and at least 3 g per day

n-3 fatty acids.<sup>2</sup> In addition to the above studies, it is important to note the influence of geography on diet. For example, residents of coastal communities are thought to have a reduced incidence of MS due to increased consumption of fish rich in PUFAs.<sup>10,11</sup> In summary, further studies are needed to clearly identify the required daily amounts of n-3 and n-6 fatty acids.

Non-steroidal anti-inflammatory drugs (NSAIDs) are predominantly used to reduce pain and inflammation, and are commonly used to treat acute exacerbations in patients with MS. As MS is thought to be an autoimmune disease and NSAIDs reduce the production of PGE2, chronic treatment with these drugs could attenuate the beneficial immunosuppressive effects of PGE2, thereby potentially aggravating the underlying disease.<sup>32</sup> As a result, MS patients on NSAID therapy must be closely monitored to ensure that disease-induced deterioration does not coincide with the introduction of NSAID therapy.

### Carbohydrate

Carbohydrate supplies fuel in the form of glucose to the brain and red blood cells. It is the primary source of energy for all body functions and is required for processing other nutrients. According to Health Canada Nutrition Recommendations for Canadians, approximately 55% of total calories should come from carbohydrates. Generally half of dietary carbohydrate is in the complex form found in starch and dextrin, and the remainder consists of simple sugars such as glucose, lactose and fructose. A lack of carbohydrate in the diet can result in fatigue; a common symptom experienced by many MS patients. Adequate carbohydrate in the diet is fundamental to maintaining energy levels and mineral balance and deters

the body from reliance on body fat stores and liver and muscle glycogen stores for energy. If glycogen stores are depleted, the body begins to break down protein to supply energy required by the brain and nervous system.<sup>41</sup>

### Protein

Protein, the body's building blocks, is required for growth, repair and replacement of tissue, collagen synthesis, formation of hormones, antibodies and enzymes, and is required for excitability and contractility of neuromuscular tissue. Protein is especially important for patients with MS who are at risk for developing pressure ulcers, or who have experienced unintentional weight loss, resulting in loss of lean body mass. The recommended nutrient intake for protein is 0.9 g/kg per day for adults, or approximately 15–20% of total energy required for immune system support and prevention of muscle wasting. The major dietary sources of protein include animal products such as meat, poultry, fish, and dairy products, excluding butter, sour cream and cream cheese.<sup>41</sup>

### Energy Requirements

The amount of energy or calories a food provides is based on the macronutrient composition. A common method of calculating a patient's energy requirements is the Harris-Benedict Equation (HBE), which takes into account the patient's age, gender, height and weight. Basal energy requirements are multiplied by an appropriate activity and/or stress factors to provide the estimated total calories required. If energy restriction or repletion regimens are desired, the basal energy expenditure may be adjusted accordingly. The HBE can be used to determine appropriate energy requirements of

patients with a variety of disease states.<sup>42</sup> Interested readers should refer to a comprehensive reference such as the Health Sciences Centre Clinical Dietetic Handbook.<sup>42</sup>

## APPLICATION OF NUTRITIONAL THERAPY IN PATIENTS WITH MS

Energy and protein requirements vary among individuals and are dependent on disease state, metabolic state, and fluctuations in weight. Special consideration needs to be given to patients with MS. Patients with a decreased appetite may experience unintentional weight loss and malnutrition. Factors that decrease appetite in patients with MS include fatigue, medications (e.g. topiramate), compromised oral intake secondary to relapse and/or dysphagia. Adequate calories and protein must be consumed to preserve lean body mass, support anabolism and protein synthesis, and promote repletion. The required calories and protein often translate into large quantities of food, which is unrealistic for consumption. The diet is, therefore, supplemented to maximize caloric intake. Furthermore, an overall deficit in macronutrients suggests inadequate micronutrient intake, therefore, a multivitamin and mineral supplement is also warranted.

When energy intake exceeds energy expenditure weight gain results. This typically occurs when mobility decreases in association with progression of disease while energy intake remains the same. Restricting intake by approximately 300–500 kcal per day will result in a 0.5–1 kg weight loss per week.<sup>42</sup> Emphasis on physical activity as tolerated by the patient is encouraged

to achieve healthy body weight.

Presently, there is insufficient literature to establish precise energy and protein requirements for patients with MS. In a recent case-controlled study, 197 newly diagnosed MS cases were recruited over a four-year period and were matched with 202 controls for age and gender. The cases had significantly lower body mass index (BMI) than the controls.<sup>5</sup> Perhaps individuals with lower BMI are at higher risk for developing MS or perhaps the disease itself is associated with a hypermetabolic state, resulting in weight loss.<sup>5</sup> With these results in mind, further studies are required to accurately assess patients' energy and protein requirements during and after exacerbations.

### Pressure Ulcers

As previously mentioned, 75% of patients with RRMS develop secondary progressive disease. As mobility and activity levels decline pressure ulcers may develop. For patients with compromised nutritional status, the problem is amplified. Protein is an essential macronutrient required for repairing and replacing tissue. Pressure ulcers range from stage I to IV in severity and energy and protein requirements are calculated accordingly with higher stress factors for more severe ulcers. Protein requirements range from 1.0–2 g/kg to 1.5–2.0 g/kg.<sup>42</sup> Micronutrients such as vitamin C and zinc are also involved in the wound healing process.

### Bowel Function

Bowel dysfunction is frequently experienced by patients with MS. Both constipation and diarrhea may occur, with constipation being more prevalent. Bowel dysfunction in MS is the result of demyelination of the

CNS pathways responsible for defecation, weakened abdominal muscles, inadequate fluid and fibre intake, medications, and decreased ambulation.<sup>43</sup> Adequate fluid intake consists of approximately two liters daily or 25–35 ml/kg for the adult population.<sup>42</sup> In addition, 25–30 g per day of dietary fibre is recommended. Insoluble fibre has the capacity to retain water, increase bulk and promote bowel regularity. The best sources of insoluble fibre include wheat bran and bran cereals, whole grain foods such as whole wheat or rye bread, and fruits and vegetables including the skins. A gradual increase in dietary fibre intake is recommended to limit gastrointestinal discomfort. If benefits are not evident with a high fibre diet, then bulk-forming supplements such as Metamucil, Ultra Fibre, Correctol or Prodiem can be used. Sugar concentrates such as sorbitol or lactulose and electrolyte lavage solutions such as Golytely act by drawing water into the intestine, resulting in a softer stool. If constipation does not resolve with these measures, then a laxative such as Milk of Magnesia or Senokot may be used.

Besides disease-induced changes in bowel function, medications such as anticholinergics (e.g. oxybutinin prescribed for bladder control), sedatives (e.g. amitriptyline prescribed for pain or depression), over the counter aluminum-containing antacids, and iron supplements can also precipitate or exacerbate constipation. As a result, the need for each drug and dose must be carefully considered.

Lack of physical activity due to disease-related limitations also contributes to constipation, in that peristalsis becomes slow and abdominal muscles become weak.

THE NUMBER OF PEOPLE TURNING TO VITAMIN AND MINERAL SUPPLEMENTS IN SEARCH OF BETTER HEALTH IS INCREASING.

An optimal time for a bowel movement is approximately 20–30 minutes after breakfast due to the stimulus of the gastrocolic reflexes. Abdominal massage, regular physical activity and a scheduled time for bowel movements may facilitate defecation.<sup>43</sup>

### Dysphagia

As the disease progresses, swallowing disorders become apparent particularly when demyelination occurs in the brain stem's sensorimotor pathways (i.e. cranial nerves VII, IX, X, XII). Ultimately, the patient's nutritional intake is compromised, resulting in weight loss, malnutrition and dehydration. Depending on the location and extent of demyelination, difficulties swallowing can worsen and improve in conjunction with MS exacerbations. Patients with MS are likely to complain of coughing and/or choking on food or liquid, the sensation of food sticking in their throat, and difficulty eating particular types of foods. It is important to ensure patients are alert during mealtimes and that distractions are removed. Furthermore, proper positioning during feeding and remaining upright for 30 minutes after meals is important. Assessment and recommendations by a speech-language pathologist regarding textural modifications of solid and liquid foods are often required in order to maintain optimal nutritional status.<sup>43</sup>

### MICRONUTRIENTS

The number of people turning to vitamin and mineral supplements in search for better health is increasing. Vitamins and minerals are essential nutrients required in small quantities for fundamental physiologic processes, including growth and metabolism. Nevertheless, caution needs to be taken to prevent toxicity or deficiency of micronutrients. An

overview of the daily requirements, and symptoms of inadequate and excess intake of selected micronutrients is included in Table 1.

### Zinc, Vitamins B<sub>6</sub>, C, E

For patients following a diet containing the suggested levels of PUFA, adequate intake of zinc, vitamin B<sub>6</sub> (pyridoxine), vitamin C and vitamin E is required. Zinc and vitamin B<sub>6</sub> are involved in the formation of delta-6-desaturase, the rate-limiting enzyme required for the n-6 and n-3 metabolic pathways. Sources of zinc include whole grains, wheat, oysters and the dark meat of turkeys and chickens. Excellent sources of vitamin B<sub>6</sub> include bananas, navy beans and walnuts, however, heating, canning, or freezing alter the availability of this vitamin. PUFA are easily attacked by free radicals, which has been associated with atherosclerosis and cancer. Vitamin E acts as an antioxidant, while vitamin C is involved in the regeneration of vitamin E. The primary source of vitamin E includes the oil from plants, whereas brightly coloured fruits and vegetables such as oranges, broccoli and strawberries are the best food sources for vitamin C.<sup>2,41</sup> As previously mentioned, zinc and vitamin C are essential in the treatment of pressure ulcers in individuals with MS who are nutritionally and physically compromised. Zinc functions to support tissue and cell growth, cell replication, and maintains skin integrity; whereas vitamin C is involved in collagen synthesis and enhances wound healing.<sup>41</sup>

### Vitamin B<sub>12</sub>

There may be an association between MS and depleted levels of vitamin B<sub>12</sub> in serum and cerebrospinal fluid. A mild degree of macrocytic anemia was observed in newly diagnosed MS

patients, indicating that this is not the result of the disease or its treatment.<sup>38</sup> Whether abnormalities of vitamin B<sub>12</sub> are responsible for the mild macrocytosis of red blood cells is uncertain. There is little data with regards to the transport and requirements of vitamin B<sub>12</sub> for nervous system function. If there are increased requirements for vitamin B<sub>12</sub>, as has been suggested, then the dose and frequency required to benefit both hematological and neurological function remains to be determined.<sup>2,41,44</sup> Sources of the vitamin include poultry, fish, shellfish, and eggs.

### Calcium

As previously indicated, low body weight, decreased ambulation and inability to perform weight bearing activity places individuals with MS at risk for osteoporosis. Inadequate calcium intake, commonly seen in adults, and chronic treatment with corticosteroids such as prednisone or methylprednisolone contribute to this increased risk. Calcium is found in dairy products such as milk, cheese and yogurt, as well as salmon and almonds. Unfortunately these foods are generally under-consumed or eliminated from the diet, especially in patients who aspire to lose weight. For optimal calcium intake, patients are advised to choose low fat, calcium-rich foods along with a calcium supplement, preferably calcium carbonate, because of its increased bioavailability.<sup>42</sup>

### UNCONVENTIONAL NUTRITIONAL THERAPIES

Unconventional therapies are growing in popularity as patients seek to alleviate their symptoms. Unconventional therapies can be described

as ‘alternative’ (i.e. used instead of conventional medicine) or ‘complementary’ (i.e. used in combination with conventional medicine) and include, among other things, herbal preparations and dietary supplements. Unconventional therapies that are low risk but clinically untested may offer positive effects; however, foregoing conventional

medical treatment, is not in one’s best interest.<sup>45</sup>

### Evening Primrose Oil

Supplementing the diet with evening primrose oil, which contains linoleic acid, provides no beneficial effects in patients with MS. One possible reason for this apparent lack of benefit may be related to an insuffi-

cient amount of linoleic acid in the product, however, appropriate doses for individuals with MS have not been established.<sup>46</sup> The proposed benefit of linoleic acid hinges on its ability to enhance the production of AA, resulting in a net immunosuppressive effect, thought to be beneficial in patients with auto-immune disorders. The oral formulation is

**Table I. Overview of recommended daily intake and symptoms of inadequate and excess intake of selected micronutrients<sup>41,42</sup>**

Micronutrient	DRI	UL (mg/day)	Deficiency	Toxicity
<b>Vitamin B<sub>6</sub></b>	M/F: 1.3 mg/d (31–50 yrs) M: 1.7 mg/d (51–70 yrs) F: 1.5 mg/d (51–70 yrs)	100	Megaloblastic anemia, diarrhea, fatigue, depression, confusion	Chronic ingestion of 2-6 g/d is associated with sensory and peripheral neuropathy and loss of myelination. Degeneration of dorsal root ganglia in spinal cord. The minimum dose at which toxicity occurs is unclear
<b>Vitamin C</b>	M: 90 mg/d F: 75 mg/d	2000	Scurvy, loss of appetite, fatigue, poor wound healing, bleeding gums	Osmotic diarrhea, kidney stones
<b>Vitamin E</b>	M/F: 15 mg/d	1000	Very rare. Retinal degeneration, hemolytic anemia and degenerative neurologic problems	Dosages of 800–3200 mg/d are associated with fatigue, nausea, diarrhea and double vision. Interferes with function of fat-soluble vitamins
<b>Vitamin B<sub>12</sub></b>	M/F: 2.4 µg/d	ND	Megaloblastic anemia, degeneration of peripheral nerves, skin hypersensitivity, glossitis	Not recorded
<b>Calcium</b>	M/F: 1000 mg/d (31–50 yrs) 1200 mg/d (51–70 yrs)	2500	Rickets, osteoporosis, osteomalacia, scurvy, parathyroid hyperplasia and hypertension	Constipation, calcium containing kidney stones. Dosages >3000 mg/d may produce hypercalcemia
<b>Zinc</b>	M: 11mg/d F: 8 mg/d	40	Poor wound healing, abnormal taste and smell, changes in hair and nails, and skin inflammation	100–300 mg/d can produce copper deficiency. 225–450 mg/d can produce metallic taste, nausea, vomiting and epigastric pain

**DRI:** Dietary Reference Intake; **F:** Females; **M:** Males; **ND:** Not Determined; **UL:** Tolerable Upper Intake Levels. The maximum level of daily nutrient intake that is likely to pose no risks of adverse effects. UL represents the total nutrient intake from food, water, and supplements, unless otherwise specified.

PHARMACISTS WORKING IN CONJUNCTION WITH A DIETICIAN WILL BE IN A  
MORE INFORMED POSITION TO ASSIST PATIENTS.

considered safe in doses of 2–4 g per day for pre-menstrual syndrome and 3–4 g per day for mastalgia.<sup>46</sup> Evening primrose oil should be avoided during pregnancy.

### Ginkgo biloba

*Ginkgo biloba* is claimed to have anti-oxidant, anti-coagulant, and anti-inflammatory properties, thereby suggesting possible benefits to MS patients. However, a study by Brochet et al.,<sup>47</sup> revealed no differences in symptom severity between patients receiving the supplement compared with those receiving placebo. As a result, *Ginkgo biloba* should not be considered effective for treating MS.

### Cranberry

Patients with MS are prone to urinary tract infections (UTI). Cranberry juice contains fructose and proanthocyanidins, which inhibit growth of bacteria in the urinary tract. Clinical studies demonstrate that cranberry juice may be effective for preventing UTIs, however cranberry juice is not effective treatment for UTIs, therefore all UTIs should be treated with appropriate anti-microbial therapy.<sup>45</sup>

### Echinacea

*Echinacea* is commonly recommended for the relief of sore throats due to colds because of its postulated immunoenhancing effects.<sup>48</sup> However, in patients with MS, stimulating the immune system may not be warranted. As a result, pharmacists must carefully consider their recommendation of this product to patients with MS.

## CONCLUSION

Nutritional intervention is a vital component in the overall management of patients with MS. Macronutrients are responsible for maintaining normal physiological function and play a

crucial role in symptom management for patients with MS and improving overall quality of life. There appears to be a consensus that following a diet low in saturated fat results in fewer exacerbations, slows deterioration, improves energy levels and reduces fatigue. Polyunsaturated n–6 and n–3 fatty acids may have immunosuppressive and anti-inflammatory effects, respectively, that benefit patients with MS. However, firm recommendations for supplementation of n–6 and n–3 polyunsaturated fatty acids have not been issued. Carbohydrate and protein are essential nutrients in maintaining energy levels, reducing fatigue and healing pressure ulcers. Further research would assist dietitians in accurately assessing energy and protein requirements for patients with MS during and after periods of exacerbation. We are aware of the importance of vitamins B<sub>6</sub>, C, and E and zinc to metabolic pathways and their antioxidant and wound healing properties. The role of vitamin B<sub>12</sub>, and the recommended dose required to correct deficiencies remains unclear. Finally, calcium plays an essential role in bone health, and through diet and supplementation, the recommended daily intake can be easily achieved. Despite the current advances in conventional medical treatment, nonconventional treatments such as herbal remedies and dietary supplements may also provide beneficial effects. Pharmacists working in conjunction with a dietitian will be in a more informed position to assist patients in the decision-making process surrounding the vast number of nonconventional products currently available. Medical treatment in conjunction with nutritional therapy can result in optimal symptom management for patients with MS.

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