

Natural Therapies for Treating Multiple Sclerosis

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Multiple sclerosis (MS) is a chronic degenerative condition that affects more women than men, with a ratio of 60 percent women to 40 percent men afflicted. This autoimmune disease attacks the nervous system. Specifically, the myelin sheaths, consisting of cells that surround nerves in the brain and spinal cord, are damaged. When the myelin sheaths are attacked they scar, or sclerose, causing various neurologic symptoms and demyelination.

Signs and Symptoms

Sufferers of MS experience a wide variety of neurologic symptoms, ranging from transient paresthesia and visual disturbances to loss of motor control of the extremities and bladder function. The symptoms classically recur with episodes of remission. Subsequent "attacks" or exacerbations usually become more frequent and worsen over time. Onset typically occurs between the ages of 20 and 40. MS is a slowly progressing disease that usually affects the quality of life more than the actual life span of the individual.

The cause of MS has yet to be determined although many theories attempt to point to a single variable. The most compelling theories, however, incorporate a number of variables as possible risk factors and causes for MS. Some of the risk factors that have been studied better include the following:

- Diet
- Genetic predisposition

- Geographic location
- Mercury toxicity
- Autoimmunity
- Viral infection
- Trace-element compartmentalization abnormalities.

The characteristic geographic clustering of MS frequency is of particular interest to investigators of the disease. People who live in tropical latitudes until age 15 rarely succumb to MS. The occurrence ratio is 1:10,000. Conversely, individuals who grow up in higher latitudes in both the northern and southern hemispheres show an increased susceptibility to the condition, with an occurrence ratio of 1:2000.¹ Young people (less than 15 years old) who migrate to tropical latitudes from higher latitudes decrease their relative risk. There are some exceptions to this distribution, primarily in Japan, where there is an overall low prevalence of MS.

Risk Factors

There are several factors that increase an individual's risk for developing MS, however, they are not confirmed as being absolute causes of the disease.

Diet

Numerous studies have attempted to link the geographic distribution of MS to the distribution of local diets. Some convincing evidence suggests that saturated dietary fats are culprits. Most higher-latitude diets are rich in animal protein and dairy foods (saturated fat), while tropical diets tend to be built around vegetable and fish protein (polyunsaturated fats). A diet that is high in saturated fat and low in polyunsaturated fats, specifically fish oils, increases the risk of developing

MS.^{2,3} This theory may also explain the low incidence of MS in Japan. The traditional Japanese diet has predominately consisted of soy and fish protein sources that are both high in polyunsaturated fats, especially omega-3 and omega-6 fatty acid oils.

Genetic Predisposition

Researchers have long noted a familial tendency, with approximately 15 percent of patients with MS having a family member, most often a sibling, being affected.⁴ Researchers have discovered a marker on the histocompatibility leukocyte antigen (HLA), a protein on white blood cells that is implicated in MS. The HLA class II allele is found more commonly in the population of patients with MS than in control subjects and may confer susceptibility.⁵ One study in particular focused on Ashkenazi Jews of Israel. This study drew a correlation between the HLA class II allele profile and disease course.⁶ This demonstrates that both genetic predisposition and genetic information may influence the course of the disease. Other markers, the HLA class I alleles, have been found to modify the expression of the HLA class II by increasing or decreasing the genetic susceptibility to MS.⁷ Recent investigations suggest that HLA molecules may be involved in the presentation of an antigen to T lymphocytes.⁸

Geographic Location

The geographic distribution of MS shows very strong clustering. Living in higher latitudes for the first 15 years of life increases an individual's risk of developing MS. However there exists no single satisfactory explanation for this distribution. As mentioned above, local dietary fat intake is one hypothesis about the distri-

A possible factor that may exacerbate multiple sclerosis is mercury toxicity, which has well-known neurotoxic effects.

tribution patterns. A second theory is based on increased production of vitamin D₃ by the bodies of people who inhabit tropical regions. Increased exposure to sunlight allows the body to convert vitamin D precursor into cholecalciferol (active vitamin D₃). Cholecalciferol is then transformed in the liver and kidneys into the most highly active form of vitamin D₃, 1,25-dihydroxycholecalciferol. This hormonally active form of the vitamin has immunosuppressive actions, specifically inhibiting autoimmune disease.⁹ In fact, exogenous 1,25-dihydroxycholecalciferol can prevent the MS equivalent completely—called experimental autoimmune encephalomyelitis (EAE)—in mouse studies. This adds support to the idea of using vitamin D₃ supplementation as a therapeutic treatment for people with MS or as preventive nutrient for those who are at risk of developing MS. Most fish oils, especially these of cold-water fish, contain substantial amounts of vitamin D₃, which could also explain why Japan is an exception to the typical pattern of MS geographic distribution.⁹ A third theory about the geographic distribution is the effect of sunlight exposure and melatonin levels. The longest and most consistent exposure of the retina to sunlight occurs in lower latitudes, resulting in reduced secretion of melatonin by the pineal gland. Reducing melatonin, an immunostimulatory neurohormone, would decrease the hyperactivity of the immune system and might reduce the risk of autoimmunity.¹⁰

Mercury Toxicity

A possible factor that may exacerbate MS is mercury toxicity, which has well-known neurotoxic effects. There is an epidemiologic correlation between MS and dental caries, which are usually filled with mercury amal-

Supplements and Dosages for Patients with Multiple Sclerosis

| Supplement | Dosage |
|--|---|
| CoQ10 | 100 mg, 1–2 times per day |
| EPA (cold pressed) | 3000 mg, 2 times per day |
| <i>Ginkgo biloba</i> (24% standardized) | 80 mg, 3 times per day |
| Glutathione (reduced) | 200–400 mg, 3–4 times per day |
| Sphingolin (myelin sheath extract) | 200 mg, 2–4 times per day |
| Oral antigen (myelin basic protein) | Dosage varies |
| N-acetyl-cysteine | 500 mg, 4 times per day |
| Selenium | 200 mcg, 1–2 times per day (total 400 mcg per day and only with a doctor's supervision) |
| Trace minerals (ionic) | 1/16 tsp equivalent, 2–3 times per day |
| Tryptophan (5-HTP) | 100 mg, 3 times per day |
| Vitamin B ₆ | 250 mg, 1–2 times per day (in a base of B-complex vitamins) |
| Vitamin B ₁₂ (methylcobalamin form) | 2 mg, 1–3 times per day orally or 1000 mcg/cc IM |
| Vitamin D | 800 IU or a prescription for calciferol |
| Vitamin E | 400 IU, 2–3 times per day |

HTP = 5-hydroxytryptophan; IM = intramuscularly; IU = international units.

gam.¹¹ A recent study compared MS sufferers with and without mercury amalgam fillings. The most striking findings were that the group with mercury fillings had significantly higher levels of depression and anger, thus, linking dental amalgam fillings and mercury toxicity with diminished mental well-being in patients with MS.^{12–14}

Autoimmunity

Numerous studies aimed at identifying a single cause for MS have been unable to do so. The most commonly accepted view is that MS is an autoimmune disease that results from an underlying genetic predisposition that can be triggered and modulated by many external or environmental factors.¹⁵

The most compelling evidence for MS being an autoimmune disease is the similarity of the central nervous system (CNS) lesions caused by animal experimental allergic encephalomyelitis (EAE) and in human MS. The lesions in MS and EAE show infiltration of the white matter of the brain and spinal cord by inflammatory cells. EAE can be induced in animals by injecting myelin basic protein, therefore, creating an autoimmune reaction to myelin. In EAE, the antigen that creates the disease is easily identified and isolated. However, in MS, the antigen has yet to be identified despite great efforts to do so.

More circumstantial evidence to support MS being an autoimmune disease is the presence of activated B and T

Even later in life, dietary essential fatty acids have been shown to be involved in myelinogenesis.

cells in the CNS lesions.⁸ This is seen via immunoglobulin (Ig) oligoclonal bands in the CSF (B-cell activation) and T-lymphocyte surface activation, but without identifying the specific antigen that is responsible.¹⁶ There are also altered ratios of T-helper to T-suppressor cells.⁴ And, finally, the use of immunosuppressants can be very effective for ameliorating the symptoms of MS for short periods of time. All of these facts point to the overall activity of the immune system causing autoimmunity.

Viral Infections

For a number of years, one popular theory of the cause of MS has invoked a latent virus that was triggered into activity by environmental factors. It is unknown whether this theoretical virus causes MS by direct damage to the myelin or if the antibody complexes created by the body end up resembling myelin. Many viral antibodies can be isolated in the CSF of patients with MS (*Herpes simplex*, measles, rubella, and *Varicella zoster*, to name a few). But the same levels of antibodies can sometimes be seen in normal subjects and in patients with a variety of other diseases. No one has answered the question of whether the antibodies are the cause of MS or a reflection of a busy immune system that has no opportunity to keep the viruses latent.

More recently, there has been speculation about the pathogenetic role of human endogenous retroviruses (HERVs) in MS.¹⁷ Perhaps HERVs contribute to the destruction of glial cells, and thus to demyelination.¹⁸ Human herpesvirus-6 (HHV-6), another retro-

virus that is commonly found in humans, follows a course of infection in early childhood and then typically becomes latent. Reactivation of this virus has been shown to occur in patients with MS and may have a part in the pathogenesis of the disease.¹⁹ HHV-6 antigens have been found in dormant, active, or fragmented forms, in a significant number of brain samples from people with MS.²⁰ The researchers also demonstrated that patients with MS have a strong and quick response to HHV-6 as evidenced by their IgM levels being significantly higher than those of subjects in a control group. This could result in polyclonal activation, the possibility of the IgM crossreacting to the proteins not only on the virus but also on the myelin cell wall.²⁰

Trace-Element Compartmentalization Abnormalities

It has been demonstrated that patients with MS have altered control over intracellular and extracellular levels of zinc and other trace elements compared to control subjects.²¹ This suggests that cellular membranes (in one study, erythrocytes) of patients with MS cannot maintain the gradient between intracellular and extracellular zinc.²² Another study reproduced these findings and found that the altered blood-brain barrier allows zinc, copper, and magnesium into the CSF of patients with MS.²³ It is unclear if this abnormal compartmentalization is a cause or an effect of the disease process. Some nutritionally oriented physicians find the use of trace minerals in an ionic form to be helpful for patients with MS.

Dietary and Nutritional Considerations

The Swank Diet

By severely restricting dietary fats, the Swank diet has been shown to improve the well-being of people with MS. Since 1948, Roy Swank M.D., a prominent neurology professor, now in private practice in Portland, Oregon, has spearheaded several studies to investigate the role of dietary fats in the progression and development of MS. When the Swank diet was implemented over a number of years, it decreased the number of attacks and impeded the advancement of MS.^{24,25} The Swank Diet reduces saturated fat intake, permits some polyunsaturated fats, encourages consumption of fish, recommends average protein intake for age and gender, and requires cod liver oil supplementation. (See box entitled The Swank Diet.)

There are a number of reasons that the Swank diet is beneficial for patients with MS.

One is the decrease of platelet stickiness or aggregation. Sufferers with MS have abnormally high levels of platelet aggregation, possibly contributing to: (1) the decrease and changes in the microcirculation of the CNS; and (2) the increased permeability of the blood-brain barrier via microemboli.^{26,27} The destruction of the blood-brain barrier over time may augment the passage of harmful components into the brain, such as viruses, bacteria, antibody complexes, and other toxic elements. The reduction of blood flow from the increased platelet aggregation promotes demyelination via direct cell death and the release of destructive enzymes.²⁸ The Swank diet has been shown to decrease platelet adhesive-

Researchers concluded that the blood of patients with multiple sclerosis showed signs of oxidation.

ness and aggregation substantially. Excessive aggregation and small clumps of platelets that can form microemboli are believed to result in the following events in patients with MS: (1) damage to the blood-brain barrier; (2) altered microcirculation for the ventral nervous system; and (3) diminished brain perfusion.

A second reason that the Swank diet is advantageous is because it decreases inflammation and the autoimmune response by increasing the essential fatty acid (EFA) levels in the blood and particularly in the CSF. There is a documented lack of EFA in the red blood cells and in the CSF of patients with MS.²⁹ EFAs are involved in the immune system and influence the production of prostaglandins, the mediators of inflammation. EFAs are precursors to prostaglandins; different EFAs lead to an increase in different prostaglandins. For example, eicosapentaenoic acid (EPA) and dihomogammalinolenic acid (DGLA) contribute to the prostaglandin-3 and -1 pathways respectively, which are both anti-inflammatory. Arachidonic acid contributes to the prostaglandin-2 pathway, which is proinflammatory. All of these EFAs compete for the same active site on the enzyme. Therefore, increasing the dietary intake of EPA and DGLA cuts down the production of proinflammatory prostaglandins and decreases the autoimmune response.^{30,31}

A third reason that the Swank diet is beneficial is the normalization of EFA levels in the blood and CSF contributing to myelin formation. EFAs are important building blocks of myelin. This is usually most important in infancy, when the majority of myelin is being formed but, even later in life, dietary EFAs have been shown to be involved in myelinogenesis.³²

Linoleic Acid

Linoleic acid is an EFA and works according to the same principles as the Swank diet works. In an analysis of three double-blind trials, researchers concluded that supplementation yielded favorable results. The patients with less disability improved more than patients with severe disability, however supplementation minimized the severity of and duration of attacks regardless of disability or period of illness.³³ The duration of treatment was more than 2.5 years. There is evidence that red-blood-cell lipids require 2 years of using supplementation to normalize.³⁴ This suggests that long-term supplementation, more than 2 years, may be needed to correct myelin lipid content because of the slow replacement rate of myelin cells compared to that of red blood cells.

Antioxidants

Antioxidants are a key factor in cellular degradation. They prevent damage by stopping oxidation and lipid peroxidation to all cells in the body. The brain and nervous system are most vulnerable to oxidative damage because of their naturally low levels of antioxidants. Studies show an increase in oxidative stress in the blood and CSF of patients with MS.^{35,36} One study investigated the blood (plasma, erythrocyte, and lymphocyte) levels of antioxidants in a population of patients with MS and how supplementation affected the levels of antioxidants. The researchers concluded that the blood of patients with MS showed signs of oxidative stress and that supplementing the patient's nutrient intake with antioxidants, such as vitamin E, ubiquinone, glutathione, and selenium can counteract this

The Swank Diet

The recommendations of the Swank

Diet are:

- 10 g or less of saturated fat per day
- 40–50 g of polyunsaturated fats per day (excluding hydrogenated oils, margarine, and shortening)
- Including fish in meals, 3 or more times per week
- Eating average amounts of protein for age and gender
- 1 tsp of cod liver oil per day

From Refs. 28 and 29.

stress and slow the progression of the disease.^{35,36} It should also be noted that any diet that is high in polyunsaturated fats (PUFAs) should include a corresponding intake of antioxidants, especially vitamin E, because PUFAs are vulnerable to lipid peroxidation.

Selenium

Selenium as an antioxidant has been studied in depth in relation to MS. There have been a number of studies that explored the increased lipid peroxidation in patients with MS and the corresponding reduction in the antioxidant enzyme glutathione peroxidase (GSH-Px).³⁷ Selenium is the mineral attached to one of the two forms of GSH-Px, and its function is to protect cell from free-radical damage. If there are low levels of GSH-Px, then the cell, in this case the myelin cell, forms more lipid peroxides leading to increased cellular damage. In studies that documented low levels of GSH-Px in patients with MS, selenium and other antioxidants increased the levels of GSH-Px in some of these patients.³⁸ Mercury toxicity can be

If there is a vitamin B₁₂ deficiency in a patient with MS, it may potentiate or aggravate the demyelination process.

diminished by selenium. Together, the two elements create a complex that has a high affinity to a specific plasma protein.³⁹

Another option is to use n-acetyl cysteine, which stimulates the liver to increase glutathione production.

Vitamin B₁₂

Vitamin B₁₂ is vital to proper nerve function. A deficiency of this vitamin, either from inadequate intake or from a lack of intrinsic factors, causes neurologic symptoms, such as paresthesia. If there is a vitamin B₁₂ deficiency in a patient with MS, it may potentiate or aggravate the demyelination process.⁴⁰ The form of vitamin B₁₂ is particularly important. In a Japanese study, 60 mg of methylcobalamin was given orally to the experiment group. The improvement was dramatic for afferent, but not for efferent, pathways.⁴¹ The results were similar to those obtained with combination high-dose IV cyclophosphamide and steroids, without the adverse side-effects. Another form of vitamin B₁₂, hydroxycobalamin, was found to be ineffective in a separate study.⁴² Methylcobalamin is the more active form that requires no conversion in order to be used in the body.

Vitamin B₆

Vitamin B₆ is another important nutrient involved in many enzyme reactions in the human body. When a deficiency is present, various symptoms can occur, most commonly depression. One theory proposed is that a deficiency of vitamin B₆ may predispose individuals to develop MS. The theory is based on evidence of carbon-monoxide poisoning, which depletes vitamin B₆, causing MS-like symptoms.⁴³ In one study, a

vitamin B₆ analogue was placed in vitro with various cell types. The researchers found that oxidative damage was reduced and improvements were seen in the MS model cells.⁴⁴

Tryptophan

Tryptophan, an amino acid, is a precursor of serotonin and other brain proteins. Plasma and CSF levels of tryptophan are often decreased in chronic MS.⁴⁵ Serotonin is metabolized quickly when an individual is under stress. Frequently, exacerbations are triggered by an increase in physical or emotional stress. In one study, patients with MS were subjected to metabolic stress by insulin-induced hypoglycemia. The results showed that they had a diminished response (adrenal cortisol reactivity, which is mediated via the serotonin system). It follows that, by increasing the availability of tryptophan, patients with MS may be less susceptible to stress and, therefore, could avoid exacerbations.⁴⁶ Another study showed an improvement in motility, bladder control, and mood with tryptophan.⁴⁷

Other Considerations

Oral Antigen Therapy

Recently, researchers have been able to reduce the symptoms, demyelination, and antibodies in EAE rats dramatically by administering oral myelin basic protein (MBP).⁴⁸ MBP, an oral protein antigen, is able to induce systemic nonresponsiveness to the antigen the animals were fed. There seem to be two separate mechanisms: active suppression and clonal depletion.⁴⁹ The dose, timing, and form

of antigen is also critically important to success. In humans, the research is being conducted with variable levels of success, however optimistic researchers may be.^{49,50}

Ginkgo Extract

As mentioned above, there is increased oxidative stress and abnormal platelet aggregation in MS. *Ginkgo biloba* has strong antioxidant properties as well as being an antiplatelet aggregator and improving blood flow to the brain. One study attempted to assess the clinical relevance of ginkgo supplementation. The study's results were not in favor of using ginkgo for short-term flareups in MS.⁵¹ However, this study lasted only 7 days, an inadequate time for a proper assessment of the herb's long-term effects.

Malabsorption

Malabsorption may be a factor that contributes to MS. In one study, 42 percent of patients with MS had fat malabsorption, 42 percent had undigested meat fibers, 27 percent had sugar malabsorption, and 12 percent had vitamin B₁₂ malabsorption.⁵² This study reflects the potential for sufferers with MS to have various subclinical deficiencies and malabsorption present.

Lifestyle Factors

There are a number of lifestyle factors that can also affect the course of MS.

Exercise and Physical Therapy

Exercise, although difficult for some patients with MS because of their fatigue, has been found to improve their quality of life and reduce their levels of disability.^{53,54} In one study, patients with

Massage can offer relief from muscle spasms and weak muscles.

MS were split into two groups. One group performed aerobic exercise, 3 times per week, for 40 minutes, and the other group refrained from exercising. At the end of 15 weeks, the exercise group reported improvement in several areas over the nonexercise group. Specifically, depression and anger scores and sickness impact profiles (social interaction and emotional behavior) improved in the exercise group. Blood-lipid levels were measured before and after the 15-week trial. There was a significant reduction in skin fold, triglyceride, and very-low-density lipoprotein levels. Strength as well as bowel and bladder control were improved.⁵⁵ Not only were strength, lipid levels and disability improved in the patients with MS, which would have been expected, but the quality-of-life factors were improved, demonstrating how a simple and inexpensive therapy can have a tremendous impact.

Massage

Massage can improve circulation and provide comfort when disability becomes advanced. Muscle spasms and weak muscles are often a burden to the patient with MS. Massage can offer relief from these complaints.

Conclusion

MS is a challenge to the conscientious health care provider. The underlying genetic predisposition, which is most likely found on HLA class II alleles, can be triggered by many factors. Other risk factors add to the possibility of developing MS. Geographic location and the related patterns of dietary consumption of saturated fats or exposure to the sun

are risk factors. There may not be a single identifiable variable but, by implementing dietary, nutritional, and lifestyle changes, an individual suffering from MS can have the best chance of mitigating the severity and symptoms of the disease. A principal tenet of naturopathic medicine promotes the idea of optimal health via education and encouragement. The treatment of a condition such as multiple sclerosis embodies the need for a comprehensive and holistic approach. □

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