Multiple Sclerosis – Functional Approaches
by David Perlmutter, MD

Multiple sclerosis (MS) is a fairly common and generally progressive disease of the central nervous system with a prevalence in the United States of approximately 350,000 cases annually. Although the onset of MS typically occurs between the ages of 10-59 years, onset as early as 2 years of age has been described. Annual expenditures for the treatment of this disease in the United States exceed $2.5 billion. While typically regarded as a cause of morbidity, more than 3,000 Americans die each year as a direct consequence of MS—a disease in which the cause has remained stubbornly elusive.

The historical attempts to identify the cause of Multiple sclerosis have been filled with bleak commentary. As Godfried Schiedam, Court Physician of Holland, reported in the 14th century when describing a disease now thought to represent MS: "Believe me, there is no cure for this illness. It comes directly from God. Even Hippocrates and Gallenus would not be of any help here." Over a century ago, the genesis of Multiple sclerosis was attributed to some form of infection. As the French physician Pierre Marie reported in his lectures of 1891: "Before concluding this enumeration, a paragraph must be devoted to unnamed infections, so frequent, so little known, I might add so much disregarded. There are no special symptoms at the onset which indicate its existence; fever is known to have occurred, prolonged discomfort with or without gastrointestinal symptoms, occasionally jaundice or pulmonary trouble, nothing else being known about the disease. In such a case, gentlemen, you must not doubt that this is certainly a case of infection, but of a kind that it has not received any definite clinical name. As regards the patients in whom insular sclerosis (Multiple sclerosis) seems to occur from the influence of injury or physical cause, my conviction is that these cases are also due to infection, but that the infection has passed away completely unperceived, while some less important but more dramatic incident has alone attracted the attention of the patient or those who are with him."

By 1998, at least 16 infectious agents had been identified as possibly causing Multiple sclerosis. Under strict scientific scrutiny, none has been found to specifically induce the disease.

But recently, the most convincing data ever presented relating infection with a specific organism to Multiple sclerosis has been reported from the Department of Neurology and Pathology, Vanderbilt School of Medicine, Nashville, Tennessee. Dr. Subramanian Sriram and co-workers, publishing their results in the July 1999 issue of Annals of Neurology, have demonstrated the presence of a specific type of bacteria in 100% of the 37 Multiple sclerosis patients they studied. As the authors reported, "The evidence of Chlamydia pneumoniae in both progressive MS and relapsing-remitting patients suggests that the infection of the central nervous system with Chlamydia pneumoniae occurs early and persists perhaps throughout the course of the disease and does not differentiate between different clinical subtypes of the disease." This purported relationship between risk for Multiple sclerosis and infection with Chlamydia pneumoniae was recently substantiated in a study appearing in the March 2003 issue of Epidemiology. In this report, Harvard researcher Kassandra Munger found a 70% increased incidence of Multiple sclerosis in women seropositive for the presence of Chlamydia pneumoniae-specific immunoglobulin G antibodies using microimmunofluorescence.

This organism, Chlamydia pneumoniae, is a fairly recent addition to the list of bacteria known to affect humans. It is now recognized as a cause of pneumonia, pharyngitis, bronchitis, and several chronic diseases. More importantly, Chlamydia pneumoniae has now been recognized as playing at least some causative role in reactive arthritis and coronary artery disease—medical conditions which, like MS, are characterized by ongoing inflammation.

The idea that Multiple sclerosis may be caused by some form of infectious agent is supported by several interesting observations. On the Faroe Islands prior to 1920, MS was essentially unknown. Subsequent to the invasion of British troops, the incidence of MS increased dramatically. This would support the contention that MS, at least on the Faroe Islands, was caused by some infectious agent to which the native population had not been previously exposed.

In addition, the cerebrospinal fluid (CSF) in patients with documented Multiple sclerosis, is typically found to contain high amounts of specific proteins known to be elevated in other nervous system disorders in which infectious causes have been clearly identified.

If there is such a strong relationship between the presence of Chlamydia pneumoniae and Multiple sclerosis, how could its presence have been missed by researchers for so many years? The answer lies in the fact that the discovery of Chlamydia in the spinal fluid of MS patients required the development of a very sophisticated test to detect a unique protein found on the cell wall of the Chlamydia pneumoniae organism itself. Indeed, this is not the first example of a profound delay in the identification of an elusive bacterium as the cause of a specific illness. It has been only in the past few years that the bacteria Helicobacter pylori has been demonstrated to be the causative agent in most cases of gastric ulcers. Incredibly, Helicobacter pylori has been identified in the stomachs of humans since the early 1980's, but medical researchers couldn't bring themselves to admit the possibility that a disease like gastric ulcers could be caused by a simple bacterium.

Another observation supporting the relationship between Chlamydia pneumoniae and Multiple sclerosis is based on the discovery that two commonly used medications for Multiple sclerosis, interferon-beta and methotrexate, profoundly inhibit the growth of the Chlamydia bacterium. This is interesting and provocative information as we don't yet fully understand why these drugs are sometimes effective in MS treatment.

Over the past several years, the medical literature has published various articles describing specific viruses thought to be the causative agent for Multiple sclerosis, only to have these reports subsequently refuted. But this new research describing the possible relationship between Chlamydia pneumoniae and Multiple sclerosis is most compelling. And the good news is that unlike viruses, specific antimicrobial medicines are available to treat Chlamydia pneumoniae.
Based upon this research, it is not unreasonable for patients with Multiple sclerosis to consider an empiric treatment for Chlamydia pneumoniae. As this discovery is so new, no specific treatment protocols have as yet been created. And it will likely be several years until clinical trials have been designed, approved, funded, completed, and ultimately published, until we know for sure that MS patients should be treated. But in light of the present evidence, empirically treating MS patients for Chlamydia pneumoniae seems reasonable. Obviously this decision should be discussed with the treating physician. Antibiotics generally quite effective in treating Chlamydia pneumoniae infections include doxycycline and tetracycline. Doxycycline may be the more effective treatment since it is more able to penetrate the blood-brain barrier to enter the brain.

Over the past two decades, well-respected researchers have described the possible link between various autoimmune diseases like Multiple sclerosis and infection with the yeast Candida albicans. In his informative book The Yeast Syndrome, Dr. John Trowbridge discussed autoimmune diseases and stated “they appear to be among the growing number of otherwise unrelated disorders partially caused by inflammation and destruction of cells, tissues, and organs, by the body’s own antibodies (auto-antibodies). These disorders belong to the autoimmune classification of diseases. Science has not explained why the body should lose the ability to distinguish between substances that are ‘self’ and those that are ‘non-self.’ An accumulating stack of evidence is pointing the finger of suspicion directly at Candida albicans, as well as other parasites or infections. How the yeast organism fosters a compromise of normal immune function is the subject of investigation and much speculation by the worldwide scientific and clinical communities.”

Because of the frequent association of Candidiasis (yeast overgrowth) with various autoimmune diseases like Multiple sclerosis, we examined 10 adult MS patients for the presence of specific antibodies directed against Candida albicans as an indicator of infection or overgrowth of this specific form of yeast. Our results, published in this journal (Townsend Letter for Doctors 148: 48-50, 1995) indicated elevated levels of immunoglobulin (one of the body’s immune proteins) against Candida, or Candida immune complexes (immunoglobulin bound to Candida) in 7 of the 10 patients evaluated.

When elevated Candida immunoglobulins are found, our next step is to perform a Comprehensive Digestive Stool Analysis (CDSA) available from Great Smokies Diagnostic Laboratory (see below). This provides information not only indicating the amount of Candida overgrowth, but in addition describes which specific non-pharmaceutical and pharmaceutical agents would be useful for treatment.

In addition to the level of Candida overgrowth and sensitivity of a patient’s Candida to various therapeutic agents, the CDSA provides other important information. Lactobacillus acidophilus is considered one of the “helpful bacteria” that normally resides in the gut. These symbiotic bacteria assist in assimilation of nutrients and produce various chemicals needed for maintenance of a healthy gut lining. In our 1995 study, 8 of 9 MS patients demonstrated significantly depressed levels of colon Lactobacillus bacteria.13 (See table 1 below).

The Dysbiosis Index is another bit of helpful information provided by the CDSA. The Dysbiosis Index essentially represents a ratio of potentially harmful bacteria divided by friendly or normal bacteria typically found in the gut, and therefore provides another indication of the status of gut health. In our study of 9 MS patients, 100% demonstrated an abnormally high Dysbiosis Index.

<table>
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Table 1. Lactobacillus count and Dysbiosis index in 9 Multiple sclerosis patients as determined by CDSA stool analysis.

From: Perlmutter, D., Fatigue in Multiple Sclerosis. Townsend Letter for Doctors 1996

Dysbiosis, an imbalance of gut bacteria, is commonly recognized in patients suffering from inflammatory diseases of the bowel. How this specifically relates to Multiple sclerosis was elegantly described in a report appearing in the highly respected medical journal, The Lancet. This study, also published in 1995, evaluated the frequency of brain MRI changes like those seen in Multiple sclerosis (white matter plaques) in patients with inflammatory bowel disease compared to normal non-affected individuals. The results of this study were profound. Hyper-intense, focal, white-matter lesions ranging from 2-8 mm in diameter were seen in 20 of 48 patients (42%) with Crohn’s disease (an inflammatory condition of the bowel), and in 11 of 24 patients (46%) with ulcerative colitis (another inflammatory bowel condition). These were patients who didn’t have MS or any other nervous system disease, just bowel inflammation. And yet, their MRI scans were identical to those of patients with documented MS! Abnormalities in the white matter were seen in only 8 of 50 (16%) healthy volunteers. As the authors reported: “The frequency of focal white matter lesions in patients with inflammatory bowel disease is almost as high as that in patients with Multiple sclerosis.”14 These findings provide convincing evidence supporting the relationship between gut abnormalities and brain pathology.

One of the most important tenets of holistic medicine holds that there is an important relationship between all of the body’s systems. Thus, focusing exclusively on controlling the immune system in the brain seems somewhat narrow-minded. New research clearly reveals a very important relationship between MS and problems in the digestive system like inflammatory bowel disease, yeast overgrowth, and low levels of healthful bacteria (Lactobacillus acidophilus). Focusing exclusively on the nervous system with MRI scans and spinal fluid analysis shortchanges the healthcare provider’s ability to gain a more comprehensive understanding of many other factors that may underlie the overactivation of the immune system.

Dietary Keys

For many years it has been known that there is a progressive increase in incidence of Multiple sclerosis with increasing latitude both north and south of the equator. For example, the incidence of Multiple sclerosis is 6-14 per 100,000 in the southern United States and southern Europe, and progressively increases to 80 per 100,000 in the northern United States, northern Europe, and Canada. A similar gradient exists in the Southern Hemisphere and is well recognized in Australia and New Zealand.

Researchers have attempted to explain this striking geographic distribution, but as yet no definitive explanation has been offered although such ideas as an “environmental factor” or a “virus” are frequently offered in textbooks.

But there are some interesting exceptions to the north/south distribution.
Multiple Sclerosis

of multiple sclerosis cases. Countries like China, Japan, and Korea, while at a similar latitude as the United States and various European countries, have a much lower incidence rate of Multiple Sclerosis. Taking a look at just one northern country, Norway, reveals that prevalence of Multiple Sclerosis actually varies quite dramatically in various districts just within that small country. Researcher Roy L. Swank, MD, PhD, provided an important observation with his unpublished research in 1952 showing that there was a direct correlation between the incidence of Multiple sclerosis in various districts in Norway and the amount of dairy products consumed by the population of those specific regions. This important, but for the most part unrecognized, discovery offered the first meaningful explanation as to why MS is so common in some areas and almost unheard of in others. Since populations living in colder climates tend to consume diets higher in fat compared to those living in more tropical regions, Doctor Swank’s theory was the first to explain the north-south distribution of MS.

Countries like Japan, Korea, and China have, until just recently, consumed diets far lower in fat than countries with high rates of MS, like the United States, Canada, and most of northern Europe. The direct relationship between MS mortality and dietary fat, especially saturated fats and animal fats was eloquently described in an extensive study involving 36 countries appearing in the American Journal of Epidemiology in 1995. In a comprehensive review article appearing in the highly respected peer reviewed journal Neurology, author Klaus Lauer, MD stated: “When the important principle of consistency is applied, however, several traits can be delineated. Both on a global scale and within smaller geographic units, the MS rate was significantly correlated repeatedly with one or another parameter reflecting the consumption of animal fat, animal protein, and meat from non-marine mammals.”

Unfortunately, while subsequent studies have continued to explore and confirm Swank’s original hypothesis, the concept that nutrition plays any significant role in Multiple sclerosis has not yet really gained a foothold in modern western medical thinking. Indeed in a recent review article entitled Management of Multiple Sclerosis appearing in the prestigious New England Journal of Medicine, the authors presented an overview of what they felt was the state of the art in treatment options for MS. Every pharmaceutical therapy from steroids to interferon, to powerful chemotherapy drugs were presented without a single mention of nutritional intervention.

Multiple sclerosis, like many other diseases of modern civilization, is a disease quite simply caused by an overactive and misdirected immune system. For reasons that remain unclear, the immune system reacts against protective insulating cover (myelin) of the nerves of the central nervous system and in addition causes damage to the actual nerve body (axon). White blood cells called lymphocytes attack myelin as if it were some invading organisms or foreign substance. When the body’s immune system fails to control itself and lymphocytes attack normal body tissue, the disease process that ensues is called an autoimmune disease. Other autoimmune diseases include rheumatoid arthritis, systemic lupus erythematosus (SLE) and even some forms of vascular disease.

The mainstay of modern western medical treatment for autoimmune diseases involves the administration of immunosuppressive drugs, designed to reduce the activity of the immune system in a general way. Indeed, this remains the focal point of treatment for acute flare-ups of Multiple sclerosis. Unfortunately, these potent drugs like cortisone, prednisone, methotrexate and cytoxan, reduce the effectiveness of the entire immune system, and are fraught with other, sometimes life threatening, side effects.

In Multiple sclerosis, lymphocytes somehow receive inappropriate signals directing them to attack the brain and spinal cord. But what are the messages which normally control lymphocytes? Their activity is regulated by a group of chemicals called prostaglandins, so named as they were originally isolated from the prostate gland. Prostaglandins can be conveniently divided into three main groups: PG-1, PG-2, and PG-3. These three groups of prostaglandins are all derived from a special type of dietary fat called essential fatty acids, or EFA’s. EFA’s are not produced in the body and hence are called essential because our survival depends on adequate nutritional sources of these critical nutrients. The two EFA’s important in the production of prostaglandins are linoleic acid and linolenic acid, part of the omega 3 and omega 6 fatty acid groups, respectively. Thus, control of lymphocyte activity, which plays a critical role in MS, is in part governed by prostaglandins, derived from nutritional sources of essential fatty acids.

The role of prostaglandins from groups 1 and 3 is to moderate or tone down immune activity and inflammation. Prostaglandins in group 2 on the other hand signal the lymphocytes to become more active in the immune response and induce inflammatory activity. In normal situations a healthy balance is achieved in immune function. Under the influence of prostaglandins from the PG-2 group, the white blood cells are activated, but this activity is kept in check by prostaglandins from groups 1 and 3. Interestingly, the cerebrospinal fluid, a liquid covering the brain and spinal cord, has been shown to contain significantly less linoleic acid in Multiple sclerosis patients compared to controls. Linoleic acid is the precursor to the prostaglandin 1 group, so its deficiency could allow overactivation of the immune system.

With the understanding that prostaglandins 1 and 3 calm the immune system while prostaglandin 2 is pro-inflammatory, the epidemiological studies describing diet and risk for MS make sense. Thus, diets rich in vegetables, nuts, seeds and fish, being good sources of linoleic and linolenic acids, favor the production of prostaglandins 1 and 3, and are associated with lower rates of MS. Diets based on animal fats, dairy products and animal proteins favor prostaglandin 2 formation and are associated with higher rates of MS, more frequent exacerbations, and higher MS-related mortality rates. It is this relationship between animal fat and immune activation that explains the observations made by Dr. Swank over 40 years ago.

What emerges from this simplified description of the regulation of the activity of lymphocytes is that it may be possible to reduce the overactivity of immune function in Multiple sclerosis by providing dietary sources of linoleic and linolenic acids, producing more of the “good prostaglandins” – groups 1 and 3. This approach to MS treatment has been followed for decades in Europe and in various Scandinavian countries where clinicians have long supported the use of EFA supplementation not only to treat the symptoms of Multiple sclerosis, but also to reduce the frequency of new events.

The reluctance of American doctors to employ essential fatty acid supplements flies in the face of substantial high quality research supporting their use, appearing regularly in our best journals. Indeed, after a comprehensive review of the current research on the subject, Columbia University’s Dr. Robert Dworkin recently stated in the journal Neurology: “The impetus for these studies was a series of
reports of a deficiency of linoleic acid in the serum of patients with Multiple sclerosis, as well as epidemiological data indicating an association between dietary essential fatty acids and the prevalence of M.S....We have reanalyzed the data from three double-blind trials of linoleic acid in the treatment of MS. Our most important finding is that patients with minimal or no disability at entry had a significantly smaller increase in disability over the course of the trials than did control patients. Additional analyses indicated that patients with minimal or no disability who were treated with linoleic acid did not have a significant change from the beginning of treatment to the end of the trial, whereas control patients had a significant increase in disability. 𝜔

In the US it is rare to find a physician who feels comfortable including essential fatty acid supplements in an MS program, especially in the face of the multi-billion dollar expenditure on the part of pharmaceutical companies to convince doctors that drugs are the only answer. Unfortunately, as has been shown by Harvard researcher Jerry Avorn, when physicians read medical journals, most of the information they retain comes not from the articles but from the advertisements. 𝜔

Any Multiple sclerosis sufferer who has explored nutritional approaches to this illness has likely discovered frequent reference to evening primrose oil. The healing power of the evening primrose plant has been known for centuries. It was used by Native Americans for infections and a variety of skin conditions. Over the past half-century, this special oil has been widely recommended in Europe as a nutritional supplement helpful in the treatment of Multiple sclerosis.

But what is it about evening primrose oil that makes it so useful in MS and other autoimmune diseases? Analysis of this oil reveals that it is a very rich source of linoleic acid which, as described above, is an essential fatty acid and the precursor of prostaglandin 1 - critically important in controlling the immune system. Other rich sources of linoleic acid are borage oil and black current seed oil. These supplements are nonprescription items, widely available in health food stores. When buying any of these oils, read labels to determine the content of GLA - the metabolite of linoleic acid that directly influences the production of prostaglandin 1.

Prostaglandin 3 is also very important in reducing the overactive immune response in Multiple sclerosis. While much less potent than prostaglandin 1, it nevertheless plays an important role by reducing the activity of inflammation enhancing prostaglandin 2. Prostaglandin 3 is derived from the other essential fatty acid, linolenic acid, which can also be supplemented in the diet. Oil of flaxseed, for example, is 50% to 60% linolenic acid. But in order to complete the process of PG-3 production, linolenic acid must first be converted to 2 important intermediate fatty acids, EPA and DHA. The conversion of linolenic acid to EPA and then to DHA is actually a fairly inefficient process. It has been estimated that under the best of circumstances humans convert only about 2.7% of administered linolenic acid to EPA. Dietary saturated fat and cholesterol reduce this conversion. In addition, the final step, converting EPA to DHA, requires a specific enzyme that may not function appropriately in a large segment of the population. So even though an individual may be taking a supplemental oil providing an adequate source of linolenic acid, it may not be contributing much of a therapeutic benefit.

But here's the good news. Various fish oil products are available which are rich in preformed EPA and DHA, eliminating the concern about the effectiveness of linolenic acid conversion. Consumption of EPA/DHA-containing fish may explain why Eskimos, who should be considered at high risk for MS because they live at far northern latitudes, hardly ever get the disease, or other autoimmune diseases for that matter. EPA/DHA supplements, like the sources of GLA described above, should be kept refrigerated to keep them from becoming rancid. Further, the idea of simply increasing fish consumption to reap the benefits of DHA is now being highly scrutinized. A recent study reported by the Associated Press has had a profound impact on the public awareness of the potential hazards of fish consumption. The report summarized research demonstrating that having as little as two servings of fish monthly led to toxic levels of mercury in 89% of the 116 subjects studied. This strengthens the case for the use of highly refined fish oils free of mercury and other heavy metals as well as PCBs.

Now let's focus on prostaglandin 2, which you'll recall enhances inflammation and immune activity. There are dietary habits that will increase production of prostaglandin 2, and may therefore prove detrimental in Multiple sclerosis. Perhaps the biggest trigger of prostaglandin 2 production is dietary fat, especially saturated fats and cholesterol (animal fats). Alcohol further enhances PG-2 production while less is produced in a diet supplemented with zinc, vitamin C, vitamins B3 and B6, and a good source of EPA/DHA (see figure 1).

This is why a low-fat, essentially vegetarian diet is critical for the Multiple sclerosis patient. In one study following 146 patients for an average of 17 years on a very low-fat diet, MS was noted to progress much less rapidly in comparison to patients not fat-restricted. There was also a significant reduction of mortality as well as frequency and severity of exacerbations of MS in the fat-restricted group. As Dr. Swank indicated, "if treated early in the disease, before significant disability had developed, a high percentage of cases remain unchanged for up to 20 years." 𝜔

Finally, about 75% of myelin is composed of fat, with a substantial amount coming from the essential fatty acids. Creating the most advantageous environment for repair and regeneration...
Multiple Sclerosis

of myelin requires an adequate supply of EFA's along with other cofactors like vitamin B12 (see below).

Nutritionists, naturopaths, chiropractors, and holistically oriented medical doctors have for years been treating Multiple sclerosis with essential fatty acid supplements, vitamins, and minerals, and fat-restricted diets, and have been doing so with great success. This approach to MS is founded on the principle of strengthening the body, working with nature, and not fighting a war using the patient as a battleground as is the case with the use of potent immunosuppressive drugs.

Antioxidant Protection

Vitamin D

Here's another reason why MS may be more prevalent in northern latitudes. Sunshine. Living further from the equator reduces the amount of sun exposure an individual may receive. Sun exposure is responsible for the formation of the active form of vitamin D which we now know has powerful antioxidant properties. That means vitamin D, like the more familiar antioxidant vitamins C, E, and lipoic acid, helps to reduce the activity of damaging free radicals - chemicals used by the immune system to destroy tissue.

In MS, increased activity of free radicals destroys the myelin covering over the nerve cells. This is why antioxidants are key players in the nutritional part of a comprehensive MS program, and why vitamin D must now be included on the list. More support for its use comes from two observations. First, as described above, MS rates are lower in populations eating cold water fish - a rich source of vitamin D.

Second, in a recent article in the journal Neurology, researchers demonstrated that on average, MS patients are severely vitamin D deficient. Unfortunately, after making this discovery the main conclusion reached by this study's authors was that because MS patients have low vitamin D levels, health care providers should watch for osteoporosis. The important antioxidant properties of vitamin D and its relevance to MS was completely overlooked.

Finally, vitamin D has been shown to completely prevent the development of a Multiple sclerosis-like disease (EAE) in the mouse model. It is this model which has been used in the development of virtually all of the pharmaceutical preparations now advocated for MS treatment. It is interesting that the severity of EAE in mice is markedly reduced by linoic acid, adding further support to its use.

Vitamin E

Like vitamin D, vitamin E is fat-soluble and freely supports the regeneration of other brain antioxidants like vitamin C, and glutathione. Adequate supplementation with vitamin E is mandatory when essential fatty acids are used to keep these delicate oils from becoming oxidized - a process which renders them therapeutically useless.

Alpha Lipoic acid

As discussed in the introduction, alpha lipoic is emerging as one of the most powerful brain antioxidants available. Readily entering the sanctuary of the brain, lipoic acid is a key nutrient in all the neurodegenerative disorders. Assisting in the regeneration of other brain antioxidants, alpha lipoic acid is a key nutrient in our protocol for MS.

Ginkgo biloba

The antioxidant power of this ancient herb is now widely recognized. Ginkgo is useful in virtually all the neurodegenerative conditions due not only to its ability to reduce the activity of free radicals, but also because of its potent effects enhancing neurotransmission, the process by which neurons are able to communicate with each other.

N-acetyl-cysteine (NAC)

By enhancing the production of glutathione, one of the most important brain antioxidants, NAC is a key supplement in MS and all other neurodegenerative conditions. As yet, there is no preformed glutathione available for oral consumption that can produce any meaningful increase in blood glutathione levels. This can be accomplished with intravenous glutathione administration (see below). Fortunately, orally administered NAC does enhance glutathione production, hence its inclusion in our protocol.

Cellular Energetics

Vitamin B12

The general lack of use of vitamin B12 in the treatment of MS by American physicians parallels their underutilization of the essential fatty acids. Vitamin B12, like essential fatty acids, cannot be patented. So it can't become an object of expensive advertising efforts in medical journals. Yet support for the use of vitamin B12 in MS treatment goes back at least to the 1950's. In 1957 German researchers published data demonstrating profound deficiencies of vitamin B12 in the blood of MS patients. Their results have been repeatedly confirmed with more recent medical publications showing low B12 levels not only in the blood, but also in the cerebrospinal fluid (CSF) of patients with MS.

One of the most important functions of vitamin B12 in humans is its role in the formation and maintenance of myelin - that all-important insulating covering over nerves of the central nervous system. Multiple sclerosis is a disease characterized by myelin destruction as a consequence of an unregulated immunological reaction. Vitamin B12 deficiency not only enhances the destruction of myelin during an MS attack, but can also compromise the body's ability to repair the damaged myelin after the storm of destruction has subsided.

In addition to the important role of this vitamin in the formation, maintenance and repair of myelin, B12 has a direct stabilizing effect on the immune system. Thus, deficiency of vitamin B12 renders an individual more vulnerable to the damaging effects of overactivity of the immune system - the fundamental flaw in Multiple sclerosis.

In an excellent review article entitled, "Multiple Sclerosis and Vitamin B12 Metabolism" published in the Journal of Neuroimmunology, Dr. E. H. Reynolds of King's College Hospital in London emphasized the importance of performing a functional assessment of vitamin B12 in the evaluation of MS patients. The test he described is simply a measurement of homocysteine. One of the functions of B12 is to keep homocysteine levels in the normal range. An elevated level of homocysteine may indicate that B12, while present in normal amounts on blood testing, may still be functionally deficient. Physicians may balk at prescribing B12 injections for MS patients with normal blood B12 levels. That's why it's important to take it a step further and request a blood test for homocysteine. If elevated (over 10 μmol/L), physicians may feel added justification in administering B12.

Almost universally our patients have felt increased energy and a better sense of wellbeing soon after beginning B12 injections. That's not surprising given the fact that B12 participates in so many chemical processes in the body dealing with energy production. In fact, combining B12 injections with oral NADH, provides a powerful antidote for the generalized fatigue that so frequently plagues MS patients. NADH acts as a cofactor for cellular energy production. The usual adult dose of NADH is 5mg
twice a day, usually taken first thing in the morning and at mid-day on an empty stomach.

**Phosphatidylserine**

Lecithin has for decades been part of complementary treatment programs for MS, and with good reason. Lecithin is one of the important building blocks for neuronal membranes, the real business end of brain cells where cell-to-cell communication takes place. Deficiencies of intracellular communication are the ultimate functional flaws in MS. Newer research has revealed that perhaps the most important component of lecithin is phosphatidylserine. Thus, adequate amounts of phosphatidylserine are required not only to preserve, but also enhance the ability of nerves to transmit information.

Phosphatidylserine plays a major role in preserving function of the membrane surrounding the energy producing apparatus of the cell, the mitochondria. Inadequacies of function of the mitochondrial membrane compromise energy production and thus threatens the viability of the neuron.

**Coenzyme Q10 (CoQ10)**

Finally, the critical role of adequate CoQ10 in facilitating cellular energy production cannot be overstated. Also known as ubiquinone because of its ubiquitous presence in all living cells, inadequacies of CoQ10 threatens the fundamental process of cellular energy production and enhances the damaging effects of naturally occurring free radicals.

**Hyperbaric Oxygen – Potent MS Therapy**

Hyperbaric Oxygen Therapy (HBOT) is without question the most exciting innovation in the treatment of MS available today. Although seemingly new on the scene, medical literature citations attesting to the effectiveness of HBOT in treating MS date back some 30 years.

Clinicians in the United States remained completely in the dark about this powerful MS therapy until 1983. In that year an article entitled “Hyperbaric Oxygen as a Treatment of Multiple Sclerosis” appeared in the highly respected New England Journal of Medicine. This report detailed the results of a 1-year study evaluating the clinical course of a group of MS patients receiving HBOT (twenty, 90-minute treatments) compared to a similar group of MS patients without the treatment. The results were remarkable. Worsening of symptoms was observed in 55% of the untreated group, while only 12% of the patients treated with hyperbaric oxygen experienced a deterioration of function. Even more dramatic was the observation that many of the treated patients actually experienced improvements in a variety of symptoms including mobility, fatigueability, tremor, bladder control, and visual symptoms. And to satisfy those who may choose to criticize the data, rest assured the study was randomized, double-blinded, and placebo-controlled.

The publication of this report created an immediate sensation. While MS patients began demanding HBOT treatment, physicians recoiled at the prospect that a non-drug therapy could prove more effective than any of the pharmaceutical approaches they had come to rely on. This prompted medical researchers to perform a much more extensive study of HBOT’s purported effectiveness in MS therapy.

In 1987 the long awaited follow-up study was completed. Evaluating triple the number of patients and using the same treatment parameters, this research, published in the Journal of Neurology, Neurosurgery, and Psychiatry, not only confirmed the results of the original report, but, in addition, revealed a striking preservation of cerebellar function (coordination) in the HBOT treatment group compared to controls.

Despite these and subsequent studies attesting to HBOT’s effectiveness in MS therapy, with the exception of a handful of pioneering souls, American physicians have continued to turn their backs on hyperbaric oxygen. Fortunately this has not been the case for most of the rest of the world.

Perhaps the largest experience in treating MS with HBOT is taking place in the United Kingdom. There, the Federation of MS Therapy Centers operates 56 hyperbaric oxygen facilities and has compiled data evaluating the progress of some 10,000 MS patients over the past 14 years. Their protocol consists of an initial course of 20 treatments over 4 weeks, followed by a single treatment on a weekly basis thereafter. Over 1 million treatments have been administered, and all without a single serious complication.

Their published results offer a direct challenge to the overall pessimistic prognoses given to MS patients in the US. Patients were evaluated on the Kurtzke scale – a measure of overall functional ability used as a standard for evaluating the progress of MS patients worldwide. None of the patients with relapsing/remitting MS who had received at least 8 treatments every 3 months experienced any deterioration on the Kurtzke scale. In fact, 40% of these patients actually improved in functional ability with treatment.

What explains oxygen’s profound benefit in Multiple sclerosis? Oxygen delivered under pressure has some important physiological effects. In the animal model of Multiple sclerosis, EAE, hyperbaric oxygen has been found to act as an immunosuppressive agent. That is, it reduces the overactivity of the immune system much like the many MS drugs, but without their dangerous side effects.

Second, by improving local tissue oxygenation, the breakdown of myelin characteristic of the immune reaction is diminished. In addition, enhanced tissue oxygenation creates a more favorable environment for myelin repair, especially in conjunction with essential fatty acids and vitamin B12.

Third, hyperbaric oxygen has been demonstrated to improve the function of the blood-brain barrier—a layer of tightly packed cells which functions to exclude potentially dangerous substances from the sanctuary of the brain. Deficiencies of the blood-brain barrier are common in MS.

**Case Report**

R.R. is a pleasant 40 year-old gentleman who was diagnosed with Multiple sclerosis some 14 years ago. Despite vigorous pharmaceutical interventions, he suffered an almost relentless downhill course, confining him to a wheelchair and making him almost totally dependent on others for his day-to-day requirements of self-care. After several months of treatment with hyperbaric oxygen at the Perlmutter Health Center, he has shown remarkable improvement. His mobility has increased, his fatigue and bladder control improved, and his overall functional ability has significantly improved.
Multiple Sclerosis

> hyperbaric oxygen therapy, his arm and leg strength improved and he regained the ability to walk with an assistive device. He writes:

Dear Dr. Perlmutter:

Regarding my positive results from hyperbaric oxygen therapy, I have noticed an improvement in energy with increased strength in my arms and less tremors in my hands. I am able to do more exercising such as sit-ups and lifting 5-pound weights. One thing very important thing to me is that my voice is stronger.

At the start of hyperbaric therapy I used a wheelchair. Now I can use the walker for most things, except for long distances. Hyperbaric therapy is relaxing, and the solitude helps with my concentration.

Thank you,
R.R.

Diet

The MS diet is essentially vegetarian. Meat products and eggs enhance the formation of inflammation-producing fatty acids. Protein sources include cold water fish and vegetable protein including soy products like tofu and soy protein powder. Dairy products should be minimized. Instead, choose soy-based cheeses and soy milk instead of cow's milk. Nuts, seeds and dark green leafy vegetables, all rich in essential fatty acids, should be emphasized. Alcohol should be eliminated since it enhances the formation of the damaging 2 series prostaglandins. When considering the possible cardiovascular benefits of alcohol, recognize that the MS diet with the supplements described below represents a potent program to reduce coronary artery disease risk. Read food product labels and reduce total fat, especially saturated fats.

**Essential Fatty Acids (EFA's)** A good source of linoleic acid is flaxseed oil. But remember, the reason for taking a linoleic acid supplement is to assist your body in the manufacturing of DHA. Since this process may be inefficient, choose products with pre-formed DHA like many of the EPA/DHA fish oil supplements. Be sure to look for fish oil supplements that have been produced in a nitrogen manufacturing environment to minimize oxidation and have undergone third party evaluation demonstrating the product to be free of heavy metals and PCBs Total daily DHA dosage should be in the range of 500 mg.

The strength of the linoleic acid supplement is determined by the GLA content. Total daily GLA dosage should approximate 300 mg. Oil supplements should always be refrigerated and taken in conjunction with a daily dose of at least 200 IU of high quality vitamin E to keep them from degrading.

**Vitamin B12.** Vitamin B12 is inexpensive and safe. Orally administered B12 is unable to achieve the therapeutic levels necessary for MS treatment. It must be given by injection. Our treatment protocol for vitamin B12 in adult MS patients begins with a daily injection of 1000 mcg (1 cc) of vitamin B12 (cyancobalamin) for 5 consecutive days followed by one injection twice weekly thereafter. Our patients are almost always able to learn how to administer these intramuscular injections themselves, generally finding the front of the thigh muscle to be the easiest injection site. Patients should receive instructions for this injection from a physician, nurse, or other qualified health-care provider. It's a good idea to alternate legs one injection to the next.

**Other Nutrients.** Vitamins B3, B6, and vitamin C, as well as the minerals zinc and magnesium reduce the formation of the inflammation-producing prostaglandin 2. Critically important antioxidants to reduce the damaging effects of free radicals generated during MS attacks include alpha lipoi acid, vitamin E, vitamin C, NAC, and Ginkgo biloba. Enhancing cellular metabolism requires adequate phosphatidylserine, coenzyme Q10, and NADH.

**Chlamydia pneumoniae.** It is very likely that this bacterium is related to MS. So it makes sense to consider empiric antibiotic treatment for *Chlamydia pneumoniae* using doxycycline. Our protocol for the empiric treatment of *Chlamydia pneumoniae* in our MS patients is: *Doxycycline 100 mg twice a day for 21 days*.

Again, the decision to engage in this empiric treatment should be made after patient and physician consider the literature linking *Chlamydia pneumoniae* to Multiple sclerosis, as well as the potential risks of taking a course of doxycycline or other antibiotic. It is always important when taking any antibiotic to also use a probiotic. These are nutritional supplements designed to reestablish appropriate levels of the "friendly bacteria" in the gut like *Lactobacillus acidophilus* and others which aid in the absorption of nutrients, help maintain the integrity of the gut lining, and assist in detoxification (see below).

**Candida.** This organism has been associated with hyperimmune diseases and specifically MS. To check for Candida, have your doctor order a Comprehensive Digestive Stool Analysis (CDSA) from

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**Perlmutter Health Center - Multiple Sclerosis Nutritional Supplement Protocol**

Vitamin B12 ........................................... 1cc (1000mcg) injected IM daily for 5 days, then twice weekly (see above)

**Essential fatty acids**

Linoleic acid - *best choice*. EPA / DHA fish oil providing .................................. DHA 500 mg
or - Flaxseed ........................................ 2 tablespoons

and, Linoleic acid: Evening Primrose oil, or Borage oil, or Black Currant oil providing .................................. GLA 300 mg

**Vitamins and Antioxidants**

Vitamin B3 ........................................... 50 mg
Vitamin C ........................................... 1000 mg
Vitamin D ........................................... 400 IU
Alpha lipoic acid .................................. 200 mg

**Cellular Energizers**

Coenzyme Q10 .................................. 60 mg
Phosphatidylserine ................................. 100 mg
NADH ........................................... 5 mg (twice)

**Minerals**

Magnesium (amino acid chelate) 400 mg
Copper ........................................... 4 mg

**Note:** The above described recommendations for essential fatty acids can be modified based on the degree of imbalance revealed in a simple blood test, the *Essential Fatty Acid Panel*, available from: Great Smokies Diagnostic Laboratory; 63 Zillicoa Street; Asheville, North Carolina 28801-9801 USA; 800-522-4762.

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TOWNSEND LETTER for DOCTORS & PATIENTS – NOVEMBER 2003
1. Dilute the appropriate dosage of glutathione liquid in 10 cc of sterile normal saline. Usually vials contain 200mg/cc, but read the label.

2. This solution is then injected through a 21-gauge butterfly catheter intravenously over a 15 to 20 minute period of time.

3. Alternatively, many patients choose to have intravenous access ports inserted. This allows frequent glutathione administration without repeated needle sticks.

4. Treatment begins at 1400mg glutathione 2 times a week and may be increased up to 2000mg 3 times a week. Our goal is to maintain the serum or urine lipid peroxide measurement in the normal range. These useful tests are available from many laboratories and are powerful indicators of antioxidant status.

Future Considerations
It is now generally well accepted that excitotoxicity plays a fundamental role in the neurodegenerative disorders, including Multiple sclerosis, as we described in the Journal of Applied Nutrition in 1999.30 (Full text available at: www.inutritionals.com/healthyliving/gslil.shtml) In this model, under the condition of intraneuronal mitochondrial insufficiency, alteration of the transmembrane potential leads to increased permeability of a specific calcium channel located on the N-methyl-D-aspartate (NMDA)-receptor. When this receptor is stimulated by the excitatory neurotransmitter glutamate, an inappropriate influx of calcium occurs which ultimately compromises mitochondrial function even further. This leads to a feed-forward cycle culminating in neuronal apoptotic death. Researchers at Albert Einstein University have recently demonstrated intense glutamate mediated axonal damage supporting this model in active MS lesions.36

Recognizing the pivotal role of glutamate stimulation of the NMDA-receptor across the spectrum of neurodegenerative diseases has prompted extensive research evaluating the therapeutic potential of interventions designed to block this receptor. Memantine is an uncompetitive NMDA-receptor antagonist. In a recent study entitled Memantine in Moderate-to-Severe...
Multiple Sclerosis

Alzheimer’s Disease, published in the New England Journal of Medicine, researchers demonstrated a significant decline in deterioration in individuals receiving Memantine, 20 mg daily, compared to the control group. Interestingly, deaths and severe adverse reactions were far more common in the placebo group compared to those receiving Memantine. The authors concluded, “This study provides evidence that modulation of NMDA receptors to reduce glutamate-induced excitotoxicity alleviated the symptoms of Alzheimer’s disease.” 37

In light of the clear demonstration that overstimulation of the NMDA receptor by glutamate is clearly implicated as having a fundamental role in axonal destruction in MS, we are now exploring the use of Memantine in this disease. It is interesting to note that glutathione also acts to suppress excitotoxic NMDA-receptor stimulation by glutamate. 38

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David Perlmutter, MD is a Board-Certified Neurologist who received his MD degree from the University of Miami School of Medicine where he was awarded the Leonard G. Rowntree Research Award. After completing residency training Neurology, also at the University of Miami, Dr. Perlmutter entered private practice in Naples, Florida where he serves as Medical Director of the Perlmutter Health Center and the Perlmutter Hyperbaric Center. Dr. Perlmutter serves as Adjunct Instructor at the Institute for Functional Medicine in Gig Harbor, Washington, and has contributed extensively to the world medical literature with publications appearing in such journals as The Journal of Neurosurgery, The Southern Medical Journal, and Archives of Neurology. He is the author of BrainRecovery.com – Powerful Therapy for Challenging Brain Disorders, and Save Your Brain (in print – Putnam Publishers, New York) and is recognized internationally as a leader in the field of nutritional influences in neurological disorders. Dr. Perlmutter has been interviewed on major M.R.I. oriented radio and television programs including 20/20, The Faith Daniels Program, and Larry King Live. He is currently involved in research at the University of South Florida studying the effectiveness of glutathione in the treatment of Parkinson’s disease. Dr. Perlmutter was awarded the 2002 Linus Pauling Award for his pioneering work in innovative approaches to neurological disorders. In addition, he received the 2002 Denham Harmon Award from the American College for the Advancement in Medicine for his work advancing the understanding of free radical biochemistry in neurological diseases.

References

15. Ibid.

Thinking of Writing a Book, but...

- You have no time • No experience •
- Don’t know where to start •
- Need a writer to work with •
- Need a sizzling proposal to attract a major publisher •
- Or need editing help for an aiming / incomplete manuscript •

Martin Zucker (818) 874-9742
Co-author: The Miracle of MSM (Putnam), Natural Hormone Balance for Women (Pocket Books), Preventing Arthritis (Putnam)

TOWNSEND LETTER FOR DOCTORS & PATIENTS - NOVEMBER 2003