Progressive Relapsing (PR) MS, which is the least common disease course, shows progression of disability from onset but with clear acute relapses, with or without full recovery. Approximately 5% of people with MS appear to have PRMS at diagnosis.

Secondary Progressive (SP) MS begins with an initial relapsing-remitting disease course, followed by progression of disability. Typically, secondary-progressive disease is characterized by: less recovery following attacks, persistently worsening functioning during and between attacks, and accompanied by progressive disability. Many patients with RRMS do develop SPMS ultimately.

Primary Progressive (PP) MS is characterized by progression of disability from onset, without plateaus or remissions or with occasional plateaus and temporary minor improvements. A person with PPMS, by definition, does not experience acute attacks. 10% of diagnosed MS are PPMS.

Relapsing Remitting (RR) MS represents 85 percent of clinical diagnoses of the disease. It is characterized by clearly defined acute attacks with full recovery or with residual deficit upon recovery. Periods between disease relapses are characterized by a lack of disease progression.

Diagnosis

No single test gives a definitive diagnosis for MS, and variable symptoms and disease course make early diagnosis a challenge. Most presumptive diagnoses of MS are based on the clinical symptoms seen in an acute attack. These presumptions are then supported by a combination of diagnostic imaging with magnetic resonance imaging (MRI), antibody testing of the fluid found in the CNS, measurements to evaluate how efficiently nerves conduct impulses (since demyelination slows nerve conduction) and evaluation of how the symptoms progress through time (D. Miller 2005).

Conventional Therapies

A cure for MS has yet to be discovered, and although recent efforts have brought advances in available treatments, substantial room for improvement remains. Presently, conventional medical treatment typically focuses on strategies to treat acute attacks, to slow the progression of the disease, and to treat symptoms.

Conventional medical treatments to treat acute disease flares

Corticosteroids
For acute MS flares, corticosteroids, such as methylprednisolone, are commonly administered in high doses to suppress the immune system and decrease the production of proinflammatory factors. These drugs are often prescribed for short periods and can be effective at alleviating the symptoms of MS. Corticosteroids should not be used for long-term therapy, however, because of their many side effects, including increased risk of infection, osteoporosis, high blood pressure, cataracts, elevated blood sugar, mood swings and weight gain. Also, while corticosteroids may reduce the symptoms of the disease, they have no effect on its progression (Virley 2005).

**Plasma exchange (plasmapheresis)**

Plasmapheresis is a process which whole blood is separated into blood cells and plasma, the liquid part of blood. In MS patients the plasma contains unusually high levels of antibodies and proinflammatory factors that exacerbate symptoms. Plasma exchange helps remove these factors quickly and is sometimes used to help combat severe symptoms of multiple sclerosis relapses in people who are not responding to intravenous steroids.

**Conventional medical treatment to modify the course of the disease**

**Beta Interferons** (Avonex®, Betaseron®) reduce inflammation and slow progression of the disease, but like many medications used in conventional medical treatment of MS, the mechanism of action is poorly understood (Yu, 1996; Heine, 2006) This specific treatment may be accompanied by adverse effects such as suicidal depression, liver damage, flu-like symptoms, and injection site reactions (Paty 2001)

**Glatiramer Acetate** (Copaxone®) is an MS treatment that yields fewer adverse side effects than beta interferon while still remaining clinically effective. Glatiramer has a chemical structure similar to the protective myelin sheath around nerves and serves as a decoy for antibodies that would otherwise attack this sheath (Ziemssen, 2007). Side effects may include flushing, rapid heartbeat, nausea, shortness of breath after injection, and injection site reactions (Sela, 2001).

**Mitoxantrone** (Novantrone®) and Fingolimod (Gilenya®) are immunosuppressants. Clinical data show that these drugs can slow the rates at which disability progresses and the rate at which new lesions form in the brain and spinal cord. These therapies, however, are not used as a first-line treatment as they can cause severe side effects including heart disease, leukemia, decreased white blood cell counts, and increased rates of infection (Fox, 2006).

**Natalizumab** (Tysabri®) is thought to block a protein that allows white blood cells to enter the brain and spinal cord and cause disease progression in MS. Due to an association with three cases of a potentially fatal infection of the CNS (Ransohoff 2005), this is a controversial drug that is only available for patients enrolled in the Tysabri Outreach Unified Commitment to Health (TOUCH) program (Warnke , 2010).
This medication is reserved for people who do not see results from other types of treatments.

**Dalfampridine** (Ampyra®) is a medication approved in 2010 that increases the ability of nerve cells to conduct impulses (Center Watch, 2011). This drug represents a new class of therapies that is aimed at addressing neurologic deficits directly.

**Medications to treat symptoms**

**Muscle relaxants:** Multiple sclerosis patients may experience painful or uncontrollable muscle stiffness or spasms, particularly in the legs. Muscle relaxants such as baclofen (Lioresal) and tizanidine (Zanaflex) may improve muscle spasticity. However, baclofen may increase weakness in the legs, and tizanidine may cause drowsiness or a dry mouth.

**Medications to reduce fatigue:** Drugs such as amantadine (Symmetrel) may help reduce fatigue.

**Other medications:** Medications may also be prescribed for depression, pain and bladder or bowel control problems that may be associated with multiple sclerosis.

**Medications on the Horizon**

There are approximately 20 experimental therapies that are on the pathway to approval by the Food and Drug Administration’s (FDA). Investigators are making progress toward developing treatments that may be capable of protecting the CNS as well as encouraging repair of brain and spinal cord lesions. Many of these drugs are potentially valuable as treatments for MS, but are months or years from traversing all phases of the FDA process.

- **Laquinimod** has been shown to decrease proinflammatory factors and increase factors that promote nerve protection without increasing risk of infection. Laquinimod was well tolerated by most patients, with only a few reports of adverse effects (Nicholas 2011).

- **Alemtuzumab** (Campath®) is an antibody specific for mature white blood cells that targets them for destruction by the immune system. This drug is approved for the treatment of certain types of lymphoma and leukemia. In one study, it was shown to be more effective than beta interferon in reducing disability progression and relapse rate, however, the trial was discontinued early due to serious side effects (Holmoy 2011).

- **Fumaric Acid** is a substance that has been used in the treatment of psoriasis and shows promise in MS to decrease white blood cell infiltration into the spinal cord (Schilling, 2006).

**Therapy and Rehabilitation to Improve Quality of Life**
In addition to one or more drug-based therapies, MS patients will often participate in rehabilitation programs intended to maintain or improve their ability to perform at home and at work. More specifically, these programs focus on general fitness and aim to address problems related to mobility, speech and swallowing, and cognitive deficits.

Common rehabilitation strategies include:

- **Physical Therapy**: Practices that aide mobility and functionality through structured physical activity on a scheduled basis.
- **Occupational Therapy**: Skills aimed at using work, self-care, and leisure activities to foster development and limit disability.
- **Speech Therapy**: Work with speech therapists can help MS patients overcome speech and language difficulties, and help with troublesome swallowing.
- **Cognitive Rehabilitation**: Assistance in managing difficulties with memory, high order thinking, and perception. A variety of cognitive rehabilitation options are available. For example, playing chess regularly is a great way to promote neuronal function and communication; computer-based “brain training” programs are also helpful.
- **Vocational Rehabilitation**: Support in making career plans, gaining job skills, and approaches to remaining gainfully employed.

**Multiple Sclerosis Nutritional Protocol**

**Overview**

Most patients that employ complementary treatments for MS do so as an accompaniment with conventional drug treatments and find both classes of therapy to provide clinical benefits (Shinto 2005). The following section outlines key details and evidence-based findings concerning the latest complementary approaches to treating MS.

**Vitamin D**

As previously mentioned, mainstream medicine has overlooked a critical missing link in MS management – vitamin D. This hormone-like vitamin is capable of safely interacting directly with the genome to modulate a variety of physiological functions, including aspects of immune function involved in autoimmune diseases like MS.

Two human clinical trials demonstrated that individuals with MS using vitamin D tended to have fewer relapses and less inflammation (Smolders 2008; Burton 2010; Wingerchuk 2005). In a one year-long Vitamin D study, recurrence rate of MS “attacks” was 27% lower compared to baseline (Wingerchuk 2005). In another large dose Vitamin D trial, MS patients given 28,000–280,000 IU weekly were found to have fewer active lesions during the 28 week long study (Kimball, 2007). In light of
the accumulating epidemiological and clinical evidence of the importance of vitamin D in this disease, supplementing the diet with vitamin D appears to be a low cost means to address this risk.

**Omega-3 Fatty Acids**

Omega-3 FAs are polyunsaturated FAs which cannot be synthesized in humans and therefore must be provided via dietary sources. Both plant and animal foods are potential sources of omega-3 FAs. For example, linolenic acid, found in flaxseed, flaxseed oil, and preferably, fish and fish oils have very high levels of EPA and DHA.

A small study looking at the effects of Omega-3 FAs on MS found that immune cells from treated patients and healthy controls produced significantly fewer pro-inflammatory cytokines after 3 months of treatment with 6 grams of fish oil per day (Gallai 1995). One double blind placebo controlled study exists to date looking at the effect of Omega-3 FAs on MS disease progression. In this study 312 patients were given either fish oil or olive oil placebo for 2 years. The results of this trial exhibited a trend toward decreased disease severity in the omega-3 FA group when compared with control (Bates 1989). More recent studies have shown that MS patients given 10g of fish oil per day for 3 months exhibited significantly reduced levels of matrix metalloproteinase-9 (MMP-9), a factor correlated with disease progression, and also had greater concentrations of omega-3 FAs in their red blood cell membranes (Shinto 2009). Other work has shown that MS patients, while on a low fat diet with omega-3 FA supplementation, experienced significantly reduced fatigue and lower relapse rates (Weinstock-Guttman 2005). Based upon clinical data and patient accounts, omega-3 FAs appear to be well tolerated and safe with no reports of adverse events.

**Linoleic Acid & Omega-6 Fatty Acids**

Linoleic acid is converted to gamma-linolenic acid (GLA), a beneficial omega-6 FA, after it is taken orally. However, this conversion is occasionally impaired, especially during inflammatory disease states (Kidd 2001; Horrobin 1997). GLA has been shown to quell inflammation and research involving an animal model of MS has demonstrated that GLA administration significantly improved clinical outcomes when compared with control treatment (Harbige 2007).

Some studies have shown significantly reduced relapse rates and disease progression scores, while others have found no differences between treatment and control groups (Harbige 2007; Bates 1977; Paty 1978). A closer look at the data from these trials revealed that patients with lower levels of disability at the beginning of the trial exhibited a smaller increase in disability over the study period than did controls. In addition, linoleic acid was found to reduce the severity and duration of MS episodes in patients at all levels of disease severity (Dworkin 1984).

**Selenium and Vitamin E**
Patients who have MS tend to have abnormally low levels of glutathione peroxidase, a powerful endogenous antioxidant (Mai 1990; van Meeteren 2005).

Researchers in Denmark conducted a small study in which patients with MS were given an antioxidant mixture containing ~2,000 mcg of selenium, 2 grams of vitamin C, and 480 mg of vitamin E, once a day for five weeks. Although glutathione peroxidase levels were initially lower in patients with MS than in normal control subjects, after five weeks of antioxidant therapy, levels of this antioxidant enzyme increased five-fold and reported side effects were minimal (Mai 1990). “... oxidative stress plays an important role in pathogenesis of multiple sclerosis. This finding, also, suggests the importance of antioxidants in diet and therapy of MS patients.” (Hadzovic-Dzuvo 2011)

**N-acetylcysteine (NAC)**

An effective strategy for increasing the body's supply of the powerful antioxidant glutathione is taking the oral supplement N-acetylcysteine (NAC), a potent antioxidant that serves as a precursor to glutathione (Kidd 2001; Arfsten 2004). NAC's potential benefit in the context of MS has been noted by some researchers (Kidd 2001; Singh 1998).

In a rodent MS model, NAC was able to to diminish clinical symptoms and pathological evidence of CNS injury, and attenuate inflammation (Gilgun-Sherki 2005).

**Lipoic Acid**

Lipoic acid (LA) is a dietary supplement with antioxidant properties and has been studied specifically in MS. Reactive oxygen species (ROS), generated primarily by immune cells, are implicated as mediators of demyelination and nerve damage (Ortiz, 2009; Miller, 2009). Known to cross the blood-brain barrier, LA decreases the activity of intercellular adhesion molecule-1 (ICAM-1), which is thought to play a role in the pathogenesis of MS. It is believed that ICAM-1 and other adhesion molecules are responsible for allowing certain pro-inflammatory immune cells, like T-lymphocytes, to enter the CNS, paving the way for induction or exacerbation of inflammation and tissue damage (Biernacki 2004; Cournu-Rebeix 2003; Dedrick 2003).

In an animal MS model, LA produced a significant reduction of demyelination and infiltration of the CNS by T lymphocytes (Marracci 2002; Morini 2004; Schreibelt 2006). Other researchers have followed up on these studies. In a pilot clinical trial, thirty-seven patients with MS were randomly assigned to receive various doses of LA (up to 2400 mg/day) or placebo. After two weeks, patients were assessed for levels of ICAM-1 and tolerability of high-dose LA. In addition to being well tolerated by patients, LA treatment was associated with reduced ICAM-1 levels and reduced T-cell migration into the CNS (Yadav 2005).
**Coenzyme Q10**

Coenzyme Q10 (CoQ10) is an antioxidant that is an essential part of healthy mitochondrial function and energy production with potential usefulness in treating MS. Decreased levels of CoQ10 are associated with many disease states, including heart disease, cancer, and neurodegenerative diseases (Bonakdar 2005; Siemieniuk 2005). CoQ10 was low in patients with MS (Syburra 1999). Several clinical trials of CoQ10 have been performed in neurodegenerative disease, such as Parkinson's disease, Huntington's disease, Alzheimer disease, Friedreich's ataxia, and amyotrophic lateral sclerosis (Spindler 2009). CoQ10 is a powerful lipid-soluble antioxidant that is also capable of regenerating the antioxidant capacity of vitamin E in the body. Based upon clinical evidence, CoQ10 appears to be well tolerated and safe with potential usefulness in the management of MS.

**Vitamin B12**

Some data suggests that patients with MS have abnormally low levels of vitamin B12 in their cerebrospinal fluid, blood serum, or both (Reynolds 1992). In fact, clinical vitamin B12 deficiency and MS share remarkably similar characteristics, occasionally rendering correct diagnosis difficult (Miller 2005). Notably, vitamin B12 plays a key role in the generation of myelin and thus, for decades, integrative physicians have prescribed B12 injections for patients who have MS.

Data suggests that patients given vitamin B12 supplements have experienced clinical improvements in their symptoms (Kidd 2001). For example, in the United Kingdom, researchers investigated the effects of 6 months of vitamin B12 (1 mg/week injection) on 138 patients with MS. The researchers concluded that the clinical course of patients with MS improved after beginning vitamin B12 treatment (Wade 2002).

**Ginkgo biloba**

Ginkgo biloba extracts are primarily composed of flavonoids and terpenoids and have been reported to have properties that can influence neural activity and improve cognitive performance. While controlled trials of the effects of Ginkgo biloba on cognitive function have generated inconsistent findings, more recent studies found encouraging results for patients with MS (Birks 2007; Birks 2009; Lovera 2007). In one study, patients received 120mg of Ginkgo biloba extract or placebo twice per day for 12 weeks. Those patients taking Ginkgo biloba exhibited improved measures of attention and reported fewer difficulties with memory.

**Green Tea – Epigallocatechin-3-gallate (EGCG)**

Epigallocatechin-3-gallate (EGCG) is one of many active ingredients of green tea that have been reported to have beneficial effects on the nervous and immune systems. In an animal study of MS, ECGC was found to prevent severity of clinical signs by decreasing inflammation and protecting nerve cells (Aktas 2004). According
to animal research, green tea has the ability to significantly increase regulatory T cells which are critical to providing balance to the immune system and suppressing autoimmunity (Wong, 2011).

**Curcumin**

Curcumin is an active component of turmeric, a popular Indian spice. Laboratory studies have demonstrated that curcumin has potent anti-inflammatory effects (Abe 1999). A research group carrying out animal studies has demonstrated exciting findings that curcumin treatment results in a significant reduction in disease severity and a reduction in duration of acute attacks (Natarajan 2002). In a follow-up study, laboratory researchers found curcumin not only suppressed disease severity, but also was associated with reduction of levels of interleukin-17 (IL-17) a cytokine that has been directly implicated in the progression of MS (Xie 2009).

**Biotin**

Biotin, a water-soluble B-complex vitamin, is sometimes referred to as vitamin B7. Biotin participates in biochemical reactions catalyzed by decarboxylase enzymes, supporting energy production and fatty acid and myelin synthesis (Shirani 2016; Sedel 2015). The Adequate Intake for biotin is 30 micrograms, and low-to-moderate amounts are common in multivitamin supplements (Elston 2016; Sedel 2016). Biotin’s role in neuron functioning is evidenced by its therapeutic effect in a rare genetic disease known as biotin-thiamine responsive basal ganglia disease (Sedel 2016). Children affected by this disease experience progressive neurological dysfunction, including speech and motor dysfunction, mental retardation, seizures, and possibly death (Tabarki 2013; Alfadhel 2013). Early treatment with biotin and thiamine (vitamin B1) appears to prevent progression in most cases (Alfadhel 2013; Tabarki 2013). More recently, researchers have been exploring biotin’s potential benefits in patients with MS.

In the first clinical trial to demonstrate the potential of high-dose biotin in MS therapy, 23 patients with progressive MS were treated with 100–300 mg biotin daily for an average of 9.2 months. While improvements were not seen for two to eight months after initiating biotin therapy—suggesting biotin may instigate a slow and progressive repair of MS-related nerve damage—vision improved in all four participants with MS-related optic nerve injury, and motor function and overall disability improved in 16 of 18 participants (89%) with prominent spinal cord involvement (Sedel 2015; Sedel 2016).

In a randomized controlled trial, 154 patients with progressive MS received either 100 mg biotin three times daily or placebo for 12 months. Thirteen (12.6%) of the biotin-treated subjects versus none of the placebo subjects exhibited improvements in measures of MS-related disability after nine months that persisted through the end of the trial. In addition, only 4.2% of biotin-treated subjects compared with 13.6% of placebo subjects had progressively worsening disability scores at nine months. At the end of the 12 months, placebo subjects were switched to high-dose biotin, and
overall stabilization of disability was seen in all subjects at a 24-month follow-up (Tourbah 2016).

Biotin levels in the cerebrospinal fluid of MS patients have been observed to be lower than those of healthy people, leading to speculation that low biotin availability may contribute to the pathology of MS (Anagnostouli 1999). Although the mechanism of biotin’s ability to prevent or repair nerve damage is unknown, biotin may prevent progressive demyelination by improving mitochondrial function, increasing brain energy production, supporting myelin production by increasing lipid synthesis, and affecting gene expression (Heidker 2016; Sedel 2016).

Biotin is excreted through the urinary system, and high doses appear to be well tolerated in trials to date (Peyro Saint Paul 2016; Sedel 2016). However, high doses of biotin may interfere with certain lab tests, including thyroid function tests, leading to misdiagnosis of thyrotoxicosis (Barbesino 2016; Minkovsky 2016; Elston 2016). In addition, the possibility of teratogenicity has been suggested by animal research (Peyro Saint Paul 2016); therefore, the safety of high-dose biotin in pregnancy is not established.

**Swank Diet**

Dr. Roy Swank first proposed a connection between increased consumption of saturated animal fat and the incidence of MS in 1950 (Swank 1950). He conducted a study which enrolled 208 patients with MS in the early 1950’s, all of whom had experienced at least two acute relapses, and followed their progress over 34 years (Swank 1990). In this study, patients maintained the now termed Swank Diet, which consists of: less than 15g/day of saturated animal fat, 10-15g/day of vegetable oil, 5g/day of cod liver oil, and one multivitamin (full details below). Long-term follow-up results from this study indicate that the patients adhering to the Swank Diet experienced reduced MS disease activity and progression of disability when compared to patients that did not follow the regimen. While these results are encouraging, this trial is criticized for its lack of a proper control group and un-blinded design. Nevertheless, the Swank Diet remains one of the most popular complementary approaches to treating MS.

**Swank Low-Fat Diet: Detailed Guidelines**

- Saturated fat should remain less than 15 grams per day
- Unsaturated fat should be approximately 20-50 grams per day
- No red meat should be consumed during the first year
- After the first year, a maximum of 3 oz. of red meat per week
- Dairy products must have 1% butterfat or less
- Processed foods containing saturated fat should not be eaten
- A source of omega-3, a multi-vitamin, and a mineral supplement are recommended daily
• Wheat, gluten or dairy product quantities are not restricted, unless they are foods which cause allergies or reactions.

**Hormone Therapy**

Because women often experience improvement of MS symptoms while pregnant, hormone therapy using estrogen has been studied as a treatment for the disease. In human studies, estriol treatment (8mg/day) in nonpregnant women with MS was associated with reduced lesion numbers and lesion volumes and when treatment ceased, these values returned to levels observed before treatment (Sicotte 2002). Patients given estriol also had enhanced cognitive function. With respect to immune studies, estriol was associated with reduced pro-inflammatory and increased anti-inflammatory cytokine production and these changes correlated well with the reduced formation of lesions (Soldan 2003).

Other studies have shown that male MS patients treated with 10mg of testosterone exhibited improved cognitive performance and reduced brain atrophy, although MRI data showed no change in lesion formation (Sicotte 2007). In another similar study, testosterone treatment in males was associated with reduced production of inflammatory cytokines and increased production of neuroprotective factors (Gold 2008).

There is currently debate among researchers about the role of hormones with MS and how that relationship may be exploited as a means of therapy. Some studies argue for hormone replacement as a new therapeutic approach (El-Etr, 2011). More information can be found in Life Extension’s protocols on Male Hormone Restoration Therapy and Female Hormone Restoration Therapy.

**Multiple Sclerosis**

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