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Breech



Anterior



Posterior



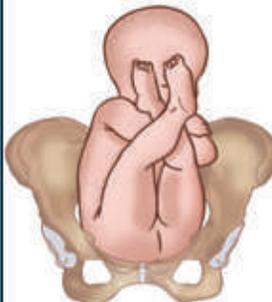
Transverse



**Outcome of breech delivery in a tertiary care centre**

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Frank Breech



Complete Breech



Footling Breech



# Antioxidants and multiple sclerosis (MS)

**SANJAY AGRAWAL, ANSHU YADAV**

Multiple sclerosis (MS) is an immune-mediated disease, with inflammation and neurodegeneration contributing to neuronal demyelination and axonal injury. Current therapies for MS are directed toward modulation of the immune response; however, there is increasing evidence that oxidative stress is an important component in the pathogenesis of MS. The inflammatory environment in demyelinating lesions is conducive to the generation of reactive oxygen species. When these species are generated in MS and animal models of MS, products such as peroxynitrite and superoxide are formed that are highly toxic to cells. There are several examples of potential beneficial effects from various antioxidants in animal models of MS, but the efficacy may vary between different agents and, in some instances, may yield deleterious effects. Despite these promising results in animal models, there is limited and conflicting evidence of potential therapeutic effects of antioxidants such as vitamins C and E in treating MS. However, clinical trials in MS patients with more potent antioxidants, identified in animal studies, have been initiated.

## Diet and MS – the big picture

Maintenance of general good health is important for people

with MS or any chronic disorder. A well-balanced and carefully planned diet will help to achieve this goal. While many different diets have been proposed as a treatment, or even a cure, for the signs and symptoms of MS, evidence of effectiveness is very limited. Most of these proposed diets have not been subjected to rigorous, controlled studies, and the few that have been evaluated have produced mixed results.

Researchers are making significant connections, however, in the story of diet and MS that may eventually impact the lives of people living with MS. Here are some key findings and some areas where the results are mixed.

### Important leads

**Vitamin D** - Research is increasingly pointing to a reduced level of vitamin D in the blood as a risk factor for developing MS, and studies are underway to determine if vitamin D levels influence MS disease activity. The National MS Society has led the way in this research, funding early preclinical studies, convening a summit on this topic, and now funding a clinical trial of vitamin D supplementation.

**Salt** – Several reports suggest that dietary salt can speed the development of an MS-like disease in mice, and provide new insights on immune system activity involved in MS. While more research needs to be done to confirm a role for salt in triggering MS, or to determine whether reducing salt can inhibit MS immune attacks, these studies pinpoint new avenues for strategies that can decrease MS attacks.

These studies were funded in part by the National MS Society, and the Society is now funding further research that explores how salt affects the immune system in humans.

**Antioxidants** – these natural or manmade substances are found in many foods. In MS, the immune system damages and destroys myelin, the material that surrounds and protects nerve fibers in the brain and spinal cord. Nerve fibers themselves are damaged as well, which appears to drive long-term disability. “Free radicals” are normal by-products of bodily processes, and may cause tissue injury and turn on immune attacks in MS. Antioxidants block the action of free radicals. Controlled trials are underway to test the potential of several antioxidants for treating MS:

- Scientists at Oregon Health Science University are testing whether oral lipoic acid can reduce optic nerve damage (often the first symptom indicating MS) in people at high risk for MS.
- Researchers at the National Institutes of Health are testing whether idebenone (a man-made drug that is similar to coenzyme Q10, a common dietary supplement) can decrease loss of brain tissue volume in people with primary progressive MS.
- Several groups are investigating antioxidants isolated from green tea in people with MS, based on studies in MS-like disease which showed that these substances can reduce the effects of the immune attack.

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### Mixed results

- Plant-based diet - A one-year study tested a low-fat, plant-based diet on measures of disease activity, mobility, fatigue, cholesterol, body weight, and compliance in 61 people with relapsing-remitting MS. Half of the participants received 10 days of diet and cooking training, while the control group was wait-listed. Results show no significant changes in MRI scans, EDSS, or mobility. Fatigue scores improved significantly. Participants showed good compliance, and were able to lose weight and reduce cholesterol levels. Although larger studies are needed, these results (presented at a medical meeting, and yet to be published in full) help to fine-tune our understanding of how managing diet may help people with MS.
- Red wine - Previous research has suggested that resveratrol, a component of red wine, enhances the activity of a molecule (SIRT1) that might help to preserve nerve fibers, and it has been shown in several studies to decrease the severity of MS-like disease in mice. At least one more recent report, however, suggests that resveratrol actually may worsen disease in mice, so additional research is needed.
- Ginkgo - Extract from the Ginkgo biloba tree has been used for a variety of medicinal purposes, and small pilot studies hinted that it might be beneficial for cognitive impairment in MS. But results of a placebo-controlled, 12-week clinical trial showed that Ginkgo biloba failed to improve cognitive function in 121 people with MS.

- Omega-3 - Polyunsaturated fats — and the omega-3 fatty acids they contain — have been the focus of MS studies with some evidence pointing to benefits for relapsing-remitting MS. But a recent Norwegian study showed that omega-3 fatty acid supplements were safe in 92 people with relapsing-remitting MS, but failed to show benefit in any clinical or quality of life measures

### 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 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; Schreiber 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). ❖

Urinary tract infections (UTI) are very prevalent in patients with diabetes mellitus (DM) and have been reported to have unfavorable outcomes. In spite of its increased prevalence, understanding about the underlying mechanisms predisposing patients with DM to UTI are unclear. Also, there is a surge in antibiotic resistance amongst uropathogens. This calls for an improved knowledge of host defenses that provide protection to the urinary tract from microbial insult in order to formulate new UTI treatment options that can improve care provided to people with DM.

**- American Urological Association**