Multiple Sclerosis and Complementary Medicine: A Brief Look

Ms. L is a 28-year-old mother and fourth grade school teacher. She has multiple sclerosis, (MS), a debilitating disease of the central nervous system. She occasionally has problems with urination and tingling and tightness in her muscles, but her main complaints are fatigue and depression. She sees a neurologist regularly and takes a disease-modifying drug. She also takes ginseng, which she read about online; she thinks it helps with her fatigue.

Mrs. T is a 42-year-old homemaker who was diagnosed with multiple sclerosis over fifteen years ago. Her symptoms are worse now than they were then. She has significant problems with pain in her muscles, muscle spasms, dizziness, and sometimes has had trouble with her vision (blindness in one eye). During flares of her disease, she sometimes has to use a wheelchair due to weakness. She sees a neurologist regularly, but is unhappy about how about how her disease has progressed, and is ready to try anything new. She takes extra vitamin D daily, because she read in a magazine that it was good for the immune system.

Mr. X is a 55-year-old attorney who was diagnosed with multiple sclerosis twenty years ago. He has had a number of symptoms over the years, but the complaint that bothers him the most is his poor memory and his difficulty concentrating. He practices yoga and meditation daily, and feels his disease flares up more when he doesn't do this.

All three of these individuals are choosing to use complementary medicine in addition to treatment by a neurologist. All are living with MS, with different symptom profiles, and all of them are looking for every way possible to lead normal, fulfilling lives.

About 400,000 individuals in this country suffer from multiple sclerosis, a debilitating neurological disease. It is a chronic disease, with an unpredictable course; though some individuals suffer only mild symptoms, in others the disease takes a more severe form. In the most common form of MS, the disease takes a relapsing/remitting course, with periods of symptom exacerbations, followed by periods of relative remission; however, the disease patterns may worsen over time, leading to symptoms which do not ever go away completely. The disease presentation is not exactly the same in any one person, since the disease can cause specific areas of inflammation and damage at any point in the central nervous system, which includes the brain,

optic nerve, and spinal cord. Individuals may suffer from muscular symptoms, including spasms, numbness, tremor, tingling sensations, problems with coordination and balance, or weakness. Nerves to the bowel, bladder, or genitals may become involved, leading to difficulties with urination, defecation, and sexual function. Involvement of the optic nerve may cause vision problems, and damage to the nerves controlling speech, chewing, swallowing, and hearing may cause difficulties with these activities. Since the brain itself can become involved, symptoms can include decreased attention span, difficulties with judgment, memory, problem solving, and dizziness; depression and fatigue are also not uncommon.

Multiple sclerosis is most commonly diagnosed in individuals twenty to forty years of age, and in women more commonly than in men. Writings as far back as the Middle Ages identify patients which neurologists now believe suffered from MS; the disease was officially identified by Dr. Charcot, one of the founders of neurology, in 1868. In 1916, Dr. Dawson was the first person to describe the demyelinization and inflammation that we now know to be integral to the disease's origin. Though the exact cause is still unknown, MS is thought to be an autoimmune disease; the symptoms of MS are thought to be triggered by damage to the myelin sheath, a specialized protective layer of cells that surround nerve cells. The body's own immune system may become inappropriately activated to attack these cells, and the resultant bouts of inflammation are thought to slow down or stop nerve impulses, causing the flares in symptoms seen in the most common form of the disease. With repeated flares, the nerves may become permanently damaged, and a given individual's symptoms may become more permanent. It is hypothesized that an unknown virus may play a role in triggering the inflammation, and genetics and certain environmental factors are known to play a role as well.

There is currently no cure for multiple sclerosis, but there are medications which can help slow the disease process. These include corticosteroids and a variety of immune system modulating drugs such as interferons (e.g., Avonex) or glatamer acetate (Copaxone). Many of these drugs entail a significant side effect profile, and some carry notable risks. Other drugs target symptomatic relief, such as drugs for muscle spasticity, fatigue, bladder dysfunction, constipation, or impotence. None of these drugs are perfect; with their potential benefits they have side effect profiles like all other drugs. Depending on the clinical status of the patient, a physician also might recommend physical therapy, occupational therapy, speech therapy, or psychotherapy.

Unfortunately, even with standard treatment by a neurologist, many individuals with MS may continue to exhibit symptoms, some of which significantly impair patients' quality of life, and even their ability to care for themselves. Research continues in the area, and multiple new drugs are currently undergoing clinical trials, while others show potential in earlier phases of drug development. But that research is not available now. The clinical evidence is not fully enough developed for any of these new potential therapies to be approved for treatment. It is perhaps not surprising, then, that many patients with multiple sclerosis turn to complementary and alternative medicine as a supplement to their care. What sorts of reasons influence this decision to pursue complementary medicine? Mostly this decision seems to come not from a rejection of conventional medicine, but from patients' desire to pursue every possible avenue in alleviating their disease. In other words, most patients view these therapies as "complementary" rather than "alternative", and pursue complementary methods in addition to conventional care by a neurologist.

The field of complementary medicine is incredibly diverse, and its therapies must be evaluated on a unique basis. The National Center for Complementary and Alternative medicine (NCCAM), a branch of the National Institutes of Health (NIH), has created an informal classification scheme for the various types of therapies, though its boundary lines can be fuzzy. These complementary and alternative medicine practices (CAM) are roughly categorized as follows:

--Natural products, such as vitamins, minerals, and herbal products
--Mind-body practices such as meditation and tai chi
--Manipulative and body based practices such as massage and spinal manipulation
--Body movement therapies such as Alexander technique and Feldenkrais technique
--"Energy" based systems such as magnet therapy and Reiki
--Whole historically alternative medical systems, such as traditional Chinese medicine or Ayurvedic medicine

The technical definition of a therapy as "complementary" or "alternative" is a matter of some debate. Historically the terms have been defined more by what they are not than by what they actually are: any forms of practices or products not considered part of conventional, allopathic medicine. The definition is somewhat inadequate, as treatments once considered "complementary" may eventually become accepted as a part of conventional medicine, usually as their safety and effectiveness becomes more rigorously established with conventional research methods.

The terms "complementary" and "alternative" also bear explanation. Technically, "alternative medicine" refers to therapies that are used in place of conventional medicine, while "complementary medicine" refers to therapies that are used in conjunction with conventional medicine. These terms, again, are fuzzy; use of one term versus another may not reveal as much

information about the modality as it may reveal information about the philosophical beliefs (and possible prejudices) of the person using the term. Whatever the term used, the use of complementary therapies is not going away. Depending partly on how it is defined, around a third to a half of the general population uses some form of CAM, and use seems to be increasing among younger populations.

The use of CAM therapies in multiple sclerosis seems to be even higher. In general, CAM use tends to be higher in women, in those with medical problems without definite cures and unpredictable disease courses, and in people who suffer significant side effects from their medications: the patient profile of MS possesses all of these qualities. The majority of these individuals are not discussing their use of these therapies with a physician. The reasons for this are numerous: individuals with MS cited lack of time with the physician, perceived negativity on the part of the physician, and perceived lack of physician knowledge on the topic. In general, some physicians have some justified concerns about the use of CAM, worrying about lack of controlled clinical trials, lack of demonstrated safety profile, and patients' wasted time and money. Supplements are much less well regulated than prescription medications, causing concerns for quality control. Dosing may be difficult to determine as well. Moreover, most physicians have had very little formal training in CAM therapies, and may feel out of their area of expertise. Because of this, some physicians may have a prejudice against CAM therapies due to ignorance alone.

Patients utilizing CAM may have a somewhat different perspective. Many patients with MS possess debilitating and unpredictable symptoms which do not completely abate with conventional medical treatment alone--these patients may seek out every possibility that might treat their symptoms, even those that have not undergone enough validated research for most

physicians. Some patients may have a bias toward CAM therapies, thinking "natural is better, and definitely safe"; they may accept anecdotal evidence more readily than physicians, who have been trained to largely disregard such evidence in favor of double blind clinical studies. In surveys, multiple sclerosis patients who use CAM usually report positive results, and such people will have a certain "prejudice" toward these therapies as well. Patients may be open to discussing CAM practices with their physicians, but may be correct in believing that physicians have a bias against CAM therapies, or at least an ignorance of them; thus the topic is never breached.

This is unfortunate given the difficulty of obtaining good information about CAM therapies in MS. A great deal more information is available about CAM therapies in general than about CAM in specific patient populations such as multiple sclerosis; what information is available is highly variable in quality and reliability, and may vary greatly from one type of therapy to another. One review of many books on CAM with multiple sclerosis sections yielded some important factual errors, including defining multiple sclerosis as a form of muscular dystrophy, or recommending immune stimulating supplements, which might actually be harmful in multiple sclerosis, an autoimmune disease. Therapies endorsed were also somewhat inconsistent between these books. Information available via the internet suffers from the same variability. I found that many of the most popular sites for general information about multiple sclerosis yielded very little information specific to CAM; what information was available tended to be cautionary in tone. Information about CAM can also be obtained from certain product vendors, who may be prone to exaggerating claims about their products. Independent practitioners of CAM such as acupuncturists or naturopaths are another source of information, but these practitioners often have limited experience specific to multiple sclerosis.

Another source of information is of course the official medical literature itself. Much of this literature is inaccessible to the public, both for difficulty in physical accessibility (e.g., requiring journal subscriptions, which the public does not possess), but perhaps more importantly in terms of background knowledge required to comprehend and contextualize technical medical papers. Though the medical literature on CAM therapies and MS is growing, at this point the pool of objective information is relatively small, especially when one considers the multiplicity of CAM therapies that have been proposed for treatment of the disease. Comparatively small though it may be, this literature may still be somewhat daunting to novices to in the area, be they conventional physicians or not.

I will provide some basic information about some of the most common CAM therapies used by patients with multiple sclerosis. This information was compiled from the medical literature and other sources utilizing the medical literature. (For more information, see citations at the end of the paper.) This list is by no means comprehensive, and the potential use of any of these therapies should be discussed with a physician.

Vitamin D

A study in 2004 showed as many as seventy-seven percent of average American adults had insufficient levels of vitamin D. Though the role of vitamin D in calcium absorption and bone health has been known for years, more recent studies have found that vitamin D affects many organs and body processes, and possesses anti-inflammatory and immunoregulatory effects.

There is increasing evidence supporting the potential efficacy of vitamin D in multiple sclerosis. For many years, it has been known that multiple sclerosis is much more common in

individuals living farther from the equator; some now think this might be related to decreased vitamin D synthesis due to decreased sunlight exposure at those latitudes. In animal models of MS, vitamin D supplementation prevents and slows the progression of the disease, while vitamin D deficiency worsens the disease. In human populations, risk of developing MS appears to be lower in those with relatively high levels of vitamin D, and in those with MS, high levels have been associated with decreased risk for attacks in a variety of studies. In other words, though the evidence is not yet conclusive, vitamin D deficiency may worsen the underlying disease process of MS. In addition, individuals with MS are prone to osteoporosis, which could be worsened by vitamin D deficiency. At this point, prospective trials with MS and vitamin D are still pending. In other words, no study has given either vitamin D or a placebo to MS patients and then monitored these groups' symptoms, seeing if the group given vitamin D group does any better.

At this point, there are no definitive guidelines for conventional physicians in the management of vitamin D in MS, though given the potential benefit and probable safety, some have recommended checking vitamin D levels of those with multiple sclerosis and treating if appropriate. Excessive amounts of vitamin D can lead to elevated levels of calcium in the blood, which can cause multiple medical problems, so it is important for patients to discuss their usage of vitamin D with a health care provider.

Antioxidants

Free radicals, also called oxidants, are highly reactive molecules that are normally formed as a byproduct of metabolism. Though they play a role in normal immune defense, in large quantities they can be quite harmful. Oxidative damage is known to be involved in autoimmune mediated tissue destruction, such as that found in MS, and it has been suggested that reactive oxygen species may play a central role in the neuropathology of MS. Antioxidants tend to

decrease the damage caused by free radicals, and can be found most commonly in Vitamin A, Vitamin C, and Vitamin E, but are also found in other products sometimes taken for this purpose, such as green tea and grape seed extract. Scientists have found that antioxidant vitamins are decreased in the bloodstream of MS patients during an attack, though data have shown their levels are comparable to normal adults at other times. There are also data from animal studies to suggest that antioxidants may be helpful. However, antioxidants are known to have certain immune stimulating effects as well. Since multiple sclerosis is a disease of inappropriate immune activation, some researchers are concerned that antioxidants might have an overall negative effect. One small study found that antioxidant use was not associated with worsening of the disease, but rigorous clinical trials of antioxidants in MS have not been performed. Currently most conventional physicians do not recommend supplemental use of vitamins, unless the individual is not able to obtain a well balanced diet, and thus cannot meet the recommended daily allowances set by the Food and Nutrition Board of the National Academy of Sciences. If people with MS opt to take antioxidant supplements, they should take modest doses, as these vitamins have known toxicities at high amounts. Each vitamin may have certain interactions or side effects, and use should be discussed with a physician.

Lipoic acid is another antioxidant and dietary substance that has some potential for MS therapy. It is an effective therapy in animal models of MS. One recent trial showed decreased changes in inflammatory markers in MS patients given lipoic acid; it appears to be relatively safe and well tolerated. Certain compounds found in green tea have been found to have antioxidant, immunomodulatory, and neuroprotective effects as well. EGCG, the active component in green tea, shows some promise in animal studies, though there have been no trials performed with MS patients. The compound has generally been considered safe, though there have been rare cases

of liver failure reported. For both lipoic acid and EGCG, results can be considered only preliminary.

Cannabis

Marijuana, derived from the plant Cannabis, is a widely used illicit substance; a synthetic form of its active constituent, a class of molecules called cannabinoids, is available as a pill for medicinal use. Though the immunological effects of cannabinoids are only partially understood, it is known that they act upon receptors in the peripheral and central nervous system and have significant interactions with the opioid system, which is involved in pain and pleasure regulation in the body. There have been a number of studies focused on the use of cannabinoids in multiple sclerosis; the majority of these have focused on spasticity, the increased muscle tone sometimes seen in MS. A review of six controlled studies found that cannabinoids improved patient reports of spasticity, though objective measures of spasticity were less convincing. There is some less complete evidence for pain, bladder difficulties, and sleep in MS; survey type studies have also shown reported improvements in depression and anxiety with cannabis use. Natural Standard, the database for peer reviewed and evidence based complementary medicine, gave a grade of "strong scientific evidence" to only one therapy of the many they reviewed in MS: cannabis. It must be emphasized that marijuana use is illegal in the US, and that smoking marijuana may have significant side effects, and may alter the effects of other drugs. (Marinol, the drug form for medical cannabis, does not need to be smoked.) None of the trials compared cannabis to other well known conventional drugs for spasticity, so it is not known if it is any more effective than other prescription drugs. Medical cannabis remains a controversial topic for reasons other

than purely medical pros and cons. If a patient uses marijuana, he should discuss this with a physician.

Ginseng

Fatigue is a huge problem for many patients with multiple sclerosis. Ginseng is a plant known in the herbal literature as increasing resistance to stress and increasing energy levels. It comes in two types: Asian ginseng (Panax ginseng), the most studied form, and Siberian ginseng (eleuthero). The active constituents in Asian ginseng have a structure similar to steroids, which are used to treat MS attacks by suppressing the immune system; however, Asian ginseng has also been shown to stimulate multiple types of immune system cells. Asian ginseng has been found to reduce complaints of stress and fatigue in the general population; however, one double blind study in MS patients failed to show any benefits on fatigue reduction. Asian ginseng may potentially interact with steroids, and both types may increase bleeding tendency, though they appear to be safe at low doses. The lack of demonstrated efficacy and potential for activating the immune system may make practitioners hesitant to recommend ginseng, and instead opt for drugs such as CNS stimulants and amantadine.

Mind body therapies and movement therapies

Exercise of any kind seems to lead to reduced functional impairment and improved energy and mood in multiple sclerosis, and multiple studies support this finding. Yoga, a system of body movements and deep breathing exercises originating in India, has undergone only limited investigation, but one study found potential benefit for yoga in decreasing fatigue in MS,

showing it performed the same as regular exercise; other studies have shown decreased anxiety and stress. A recent randomized trial showed improvement in quality of life, depression, and fatigue after mindfulness training in patients with MS. Tai chi, the practice of slow, rhythmic movements made with awareness, was developed in China hundreds of years ago; it was also found to have potential benefits in a small study. Massage is another relatively safe therapy that may have several benefits, including a reduction in stress, anxiety, pain, and depression; it should be avoided over areas of recent injury and in certain other health conditions. Biofeedback is another interesting category of mind-body therapy, which shows some promise for treatment of bowel incontinence, though results are preliminary. Reflexology has shown some potential for alleviation of multiple symptoms in MS, though there have been methodological problems with many of these studies.

Except for exercise alone, all of these therapies have been studied in only a few small trials in combination with multiple sclerosis. Though the possible physiology of these various therapies is not completely known, and beyond the scope of this paper, it is well known that there are a variety of effects that the nervous system has on the immune system. Meditation and other relaxation methods seem to produce changes in immune function, though these effects are not well categorized. It is a well established fact that exacerbations of multiple sclerosis are stress related; thus decreasing psychological stress may have effects on the disease process itself. Generally these treatments are low to moderate cost and offer low potential risk; most patients with MS who utilize these therapies report satisfaction with them.

The above discussion can only be considered an introduction, and cannot serve as an endorsement of any particular CAM therapy. For more information, I recommend the Natural

Standard Integrative Medicine Database, and the National Center for Complementary and Alternative Medicine websites. I also highly recommend the book, Complementary and Alternative Medicine and Multiple Sclerosis, written by a neurologist; his website yields much of the same information. The same author has written several pamphlets for the National Multiple Sclerosis Society about CAM practices; these are available at the National MS Society website.

Here is some general advice for those patients considering using CAM therapies:

--Discuss your use of CAM therapies with your physician.

--Learn all that you can, recognizing that information varies widely on websites and books. **Recognize that information about most forms of CAM is incomplete.** Be a thoughtful consumer of information, recognizing that every source has its bias, and that consumer sources of information on CAM therapy may or may not be reliable.

--While learning, pay special attention to risks associated with a given therapy, and realize that not all of these may be known.

--If you choose to use supplements, use high grade supplements, such as those labeled with the United States Pharmacopeia symbol (USP) or the National Formulary (NF).

Some of the issues surrounding complementary medicine are complicated, both for physicians and for patients. One of its most difficult aspects concerns the difficulty in obtaining reliable information on the various therapies involved. As the previous examples illustrate, some of these therapies do have some therapeutic evidence for their efficacy beyond strictly anecdotal evidence, though in most cases the evidence in not significant enough for most allopathic practitioners to prescribe these therapies at this time. Presumably, though, this might change with further layers of evidence. For physicians, it is worth remembering that lack of incontrovertible evidence of efficacy is not proof of inefficacy. With some of these therapies, the proper studies have not been performed. For others, such as massage or yoga, truly blinded control trials are very difficult to construct. It is a bit of a conundrum: their effectiveness may be

difficult to demonstrate definitively, but that difficulty is not proof of their ineffectiveness. The practice of medicine is, of course, an evolving process; practices than were standard ten or twenty years ago are continually updated or discarded altogether; some treatments once considered "complementary" have now become a more or less accepted part of medical practice. Even if some of the effects noted by users of CAM therapies are due to the placebo effect, that doesn't necessarily mean they are worth rejecting out of hand. Some of the effects of CAM therapies probably ARE due to placebo response, just as placebo is a powerful factor in conventional therapies alone.

How should physicians and patients work through the various issues surrounding complementary therapies? There is probably no one right answer to this question, but at the very least we could begin with increased discussion of complementary medicines between patients and physicians. The National Center for Complementary and Alternative Medicine has recently initiated "Time to Talk," an educational campaign to encourage further communication between patients and physicians on this topic. As noted earlier, currently most individuals using CAM therapies do not discuss these therapies with either a physician or CAM practitioner. This is problematic for a number of reasons. Patient and physicians need to discuss possible side effects and interactions of CAM therapies. Physicians are in a prime position to help patients sort through the vast array of information on a topic and discuss what is actually known about a therapy from a medical perspective. On another level, even if a physician's advice is not followed, increased communication can enhance patient rapport and increase mutual respect between patient and physician.

It is important for physicians to recognize that patients may have a different perspective than they do, and the same information may help patients communicate more effectively with

their physicians. Physicians are highly motivated to first "do no harm"; they are highly motivated to use extreme caution in pursuing therapies which are less well categorized and unproven. Physicians are medically and legally liable for their advice; some may fear going outside the standard of care. Physicians may be less open to CAM therapies due to their training, though this varies from physician to physician, and also may change as medical school curriculums begin to give students more exposure to CAM therapies. A physician may require several well developed large prospective clinical trials before pursuing "complementary therapies", whereas patients may want to pursue therapies that have been found promising only in animals, or only in small clinical trials, especially if they appear relatively safe and inexpensive. Patients may be highly motivated to try ANYTHING to relieve their condition, and may underemphasize risks. The situation may improve as physicians educate themselves about CAM therapies and can draw upon a greater knowledge base to inform their care and advice. Though not as plentiful as one might like, resources and training opportunities are growing for conventionally trained physicians to receive appropriate, evidence based knowledge in these areas.

Though much remains to be discovered about the cause and potential therapies for multiple sclerosis, we have made amazing strides in our understanding and treatment of the disease in the hundred and fifty years since Dr. Charcot described it. Slowly, surely, we will make progress, and some of that progress will probably result from further research into various forms of CAM therapy, as we learn more about their effects. We know a great deal, but it is important to recognize how much we do not know. My own opinion is that it is best to keep a thoughtful but open mind about these therapies, weighed with evidence. As this evidence comes

in, it will be exciting to see which “complementary” therapies may be found clinically ineffective for MS, and which ones may become cornerstones of conventional care.

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