

THE WAITING ROOM

THIS WAY IN

New Guideline for Alternative and Complementary Medicine for Multiple Sclerosis

BY DARRACH DOLAN

According to the National Institutes of Health, almost 40 percent of adult Americans use complementary or alternative medicine (CAM). Americans spent \$33.9 billion on CAM in 2007 alone, according to the Centers for Disease Control and Prevention. People with multiple sclerosis (MS) are even more likely than the average American to avail themselves of CAM, with some studies estimating their CAM usage as high as 80 percent.

MS is an inflammatory disease of the central nervous system that causes a wide range of symptoms—from mild to debilitating. These symptoms can include fatigue, muscle stiffness and pain, cognitive impairment, difficulty balancing or walking, blurred vision, and tingling or burning sensations not unlike pins and needles.

WHAT IS COMPLEMENTARY AND ALTERNATIVE MEDICINE?

CAM includes the enormous range of nonconventional therapies, supplements, and practices that claim to alleviate symptoms of a disease or to improve health. They may be used in addition to (complementary) or instead of (alternative) physician-recommended therapies.

Some CAM therapies are recommended by physicians, as enough evidence has accumulated to support their use. Folic acid supplementation is often prescribed to pregnant women, and many neurologists recommend vitamin D supplementation for people with MS. Exercise is regularly prescribed by physicians to help improve the symptoms of several neurologic conditions, including MS. Hospitals often incorporate massage therapy, meditation, and visualization techniques to alleviate pain or help with rehabilitation.

Because so many CAM treatments are available and so many MS patients use them, the American Academy of Neurology

(AAN) convened a panel of experts to review studies of CAM therapies in MS, evaluate those studies based on the strength of their evidence, and issue a guideline for physicians and patients. Medical evidence should be based on large studies that include many people. When appropriate, the studies should be “double-blinded,” which means neither the researchers nor the participants know who is receiving the actual treatment and who is receiving a placebo. In addition, studies should be “randomized,” which means that participants are assigned randomly (in a sense, by coin toss) to receive either the treatment or a placebo. The effects of the treatment should be clearly measured and not left to interpretation by the researchers. If more than one study produces similar results, the treatment recommendation is considered even more reliable.

The goal of the CAM in MS guideline was to draw attention to the existing evidence for the effectiveness or ineffectiveness of CAM therapies and to highlight the need for more rigorous studies into the safety and efficacy of CAM, according to lead author Vijayshree Yadav, M.D., associate professor of neurology and clinical director of the MS Center at Oregon Health and Science University in Portland.

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EVIDENCE FOR CAM THERAPIES' EFFECTIVENESS IN MS

The key message of the guideline, according to Dr. Yadav, is that “right now, there is little evidence for the effectiveness of most CAM therapies we evaluated.” (To read a Patient Page from the American Academy of Neurology on the guideline, go to bit.ly/1cuzlVF.)

“In addition, we found that studies of the safety of CAM treatments were limited and that the long-term safety of CAM treatments is unknown,” Dr. Yadav adds. Furthermore, very



little data are available on how CAM therapies interact with conventional therapies or what the long-term effects of many treatments are.

However, lack of proof that a treatment is effective is not the same as proof that the treatment is ineffective. Future studies may offer more evidence one way or the other. "It's clear that we need much more research in the field," Dr. Yadav says.

CAM VERSUS CONVENTIONAL MEDICINE?

Barbara S. Giesser, M.D., a neurologist at University of California at Los Angeles' Reed Neurological Research Center and a Fellow of the AAN, says many of her patients use CAM therapies. "I have seen patients' symptoms improve with some CAM therapies when they are used in addition to the conventional treatments or for specific symptom alleviation. If they are not harmful to patients, I have no problem with them," Dr. Giesser says. However, she does caution against hot yoga, as MS patients can be sensitive to heat.

Both Drs. Yadav and Giesser are wary of CAM therapies with unknown side effects or unknown ingredients. "It's quite common for a patient to tell me he is taking a supplement but that he has no idea what it contains or whether the claims made by the manufacturer are supported by scientific evidence," Dr. Giesser says. Also, supplements might interact with disease-modifying therapies or other drugs prescribed for symptom management, she says. "I'm pleased that the AAN has reviewed the available literature and concluded that more studies are needed," Dr. Giesser notes.

It is vital for patients and physicians to distinguish between disease-modifying therapies and symptom-alleviating therapies, both doctors say. Disease-modifying therapies positively affect the course of the disease, whereas symptom-alleviating therapies offer relief for specific symptoms of a disease. "I don't know of any CAM treatments that affect the course of MS. So whether or not they use CAM, patients should not stop using the FDA-approved drugs that have been proven in clinical trials to reduce inflammation and relapse and slow the progress of the disease," Dr. Giesser says.

Disclosures: Dr. Yadav serves as a section editor for *Current Neurology and Neuroscience Reports*; served as consultant for Bayer Healthcare Pharmaceutical; is on the speakers' bureau of Novartis; receives research support from the McDougall Foundation, National Multiple Sclerosis Society (NMSS) Foundation, Nancy Davis Center Without Walls Foundation, Biogen Idec; and has received travel funding from the Neurological Society of India. Dr. Giesser has received support in the form of equipment to conduct a trial of a cooling device from Avacore Technologies and her husband has stocks in Biogen Idec.

VALENTYNOLKOV/ISTOCKPHOTO

CAM Therapies Shown to Be Effective

Ginkgo Biloba: This supplement is possibly effective for the relief of fatigue in MS, the guideline authors found. "However, we don't have a good handle on how ginkgo biloba alleviates this symptom," Dr. Yadav says.

Cannabis: The panel reviewed 20 studies on the effects of cannabis in different forms. "It is important to note that most of the clinical trials involved standardized derivatives of cannabis or synthetic forms of cannabis not currently approved by the FDA for use in MS," Dr. Yadav says.

Also, cannabinoids have a potential for adverse cognitive or psychological effects, such as confusion and anxiety, and the long-term side effects of cannabis use are not known at this time.

Oral cannabis extract (OCE) and tetrahydrocannabinol (THC) were found effective for patient-reported spasticity and pain in the short term, the guideline authors found. (Spasticity is a term for muscle stiffness and rigidity, a common and sometimes disabling symptom of MS.) OCE and THC were also found to be probably ineffective for alleviating tremor, but they are possibly effective for spasticity and pain in the long-term.

Sativex oromucosal cannabinoid spray, an oral spray available in Canada and some European countries but not available in the United States, is probably effective for short-term patient-reported spasticity, central neuropathic pain, and urinary frequency, according to the guideline.

(Smoked cannabis had too little data available to support or determine its safety or efficacy when used for spasticity, pain, balance and posture, and cognition.)

Reflexology: This CAM treatment, which involves applying manual pressure to points on the feet, is possibly effective for MS-related paresthesia, the guideline authors found. Paresthesia is similar to pins and needles; a person with MS may feel burning, prickling, or itching sensations on the skin. Dr. Giesser says that this is one CAM she would consider prescribing as an alternative to conventional treatments in cases where the conventional treatments have adverse side effects for a patient.

Magnetic Therapy: The guideline authors found that magnetic therapy is probably effective for fatigue, a common symptom of MS. In magnetic therapy, patients are exposed to low frequency, pulsed electromagnetic fields on a regular basis. In one study, patients lay on an electromagnetic mat for 8 minutes twice a day for 12 weeks. It is unclear how magnetism works to relieve fatigue, but it has few side-effects and is regarded as relatively benign.



NEUROLOGY NEWS

Scientists Set Parkinson's Research Goals

BY PEGGY EASTMAN

In January 2014, scientists, doctors, patients, and advocates convened at Parkinson's Disease 2014, a conference sponsored by the National Institute of Neurological Disorders and Stroke (NINDS). The goal of the conference was "A cure for tomorrow, care for today," says conference chair Thomas J. Montine, M.D., Ph.D., professor and chair of the department of pathology at the University of Washington in Seattle.

This is an exciting time for research on Parkinson's disease (PD) and other brain disorders because of the President's Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, according to NINDS Director Story C. Landis, Ph.D. The NINDS will use many of the recommendations discussed at the January conference to decide which new research projects to fund. "What would be a real success is a new therapy that slows disease progression," Dr. Landis says.

Up to one million Americans have PD, according to the National Parkinson Foundation (parkinson.org). The disease, which destroys nerve cells (neurons) in the brain, causes slowness in movement, stiff walking or "freezing," problems with balance, and hand tremors when the hands are at rest. No cure exists.

The following are key research goals in PD, according to experts who attended the conference.

GOAL: STUDY WAYS TO PREVENT OR SLOW PD

No screening test exists to diagnose PD early. Therefore, one important goal is to identify people at high risk of the disease—such as those with genetic mutations, heavy exposure to a toxic substance in the environment (certain pesticides, for example), or accumulations of a protein called alpha-synuclein in their brains—with the hope of prevention. "Identifying people at high risk of PD could allow researchers to focus on delaying its onset," says Werner Poewe, M.D., professor of neurology and director of the department of neurology at Innsbruck Medical University in Austria.

Researchers are actively searching for biomarkers—telltale biological signs that show up on blood, urine, or imaging tests—that could be used to identify and track people at higher risk of PD. "Ideally, we need a biomarker for PD that changes over time,"



says Caroline M. Tanner, M.D., Ph.D., director of clinical research at the Parkinson's Institute in Sunnyvale, CA. For example, if research confirms that a rising level of alpha-synuclein in the brain is a risk factor for PD, a biomarker for alpha-synuclein accumulation over a period of years might be useful in the clinic, much as doctors use increased cholesterol levels to identify an increased risk of heart disease in patients.

Several speakers compared brain accumulation of the protein alpha-synuclein in PD to brain accumulation of the protein beta-amyloid in Alzheimer's disease. However, it is not yet known how important alpha-synuclein will prove to be as a biomarker for PD. The NINDS considers PD biomarkers so important that it funds the NINDS Parkinson's Disease Biomarkers Program aimed at identifying high-risk people, tracking PD progression, and speeding up the development of new treatments, according to Dr. Landis.

The commonly prescribed drug levodopa, which increases the amount of a key chemical messenger called dopamine in the brain, can reduce many symptoms of PD. However, it does not stop the disease from progressing. "We are fortunate to have a number of effective options—including drugs, exercise, and surgical approaches—that relieve the symptoms of PD. But the holy grail is finding an approach that slows the underlying progression of the disease. Nevertheless, we should judge all therapies by their ability to result in meaningful benefits for people with PD," advises Lisa M. Shulman, M.D., professor of neurology and director of the Maryland Parkinson's Disease and Movement Disorders Center at the University of Maryland School of Medicine and Fellow of the American Academy of Neurology. "We need to include patient-reported outcome measures in research studies. This is the only way to ensure that the outcome of medical treatments is experienced as a benefit from the patient's perspective," says Dr. Shulman.

In addition to hoped-for new drugs, one exciting technology for PD patients is deep brain stimulation (DBS), which makes use of an electrode that is surgically inserted into areas of the brain involved in the disease. While DBS can help with movement problems, it does not slow progression of the disease. Scientists need a much clearer understanding of how DBS works before the surgical treatment can realize its promise as therapy for patients. NINDS is currently funding research to determine the safety, reliability, and effectiveness of DBS.

ANDRII KONDIUK/SHUTTERSTOCK

GOAL: STUDY NON-MOTOR PD SYMPTOMS

Participants of the conference stressed the need for more clinical studies on the non-motor symptoms of PD such as cognitive impairment and psychosis. Substantial cognitive impairment with PD is called PD dementia or Lewy body dementia. In both conditions, Lewy bodies (protein clumps that are a telltale sign of PD) containing alpha-synuclein are found in abundance in the areas of the brain involved in memory and thinking. Problems with memory and thinking may result in significant disability.

GOAL: STUDY STEM CELL LINES

Speakers at the conference discussed in detail the widely hailed promise of induced pluripotent stem cells—which can be made to turn into any cell type in the body—in helping people with PD. Currently, researchers are taking these stem cells from people with PD and coaxing them into becoming dopamine neurons in the laboratory in order to test possible new therapies, says Dr. Landis.

It is likely that research on induced pluripotent stem cell lines will lead to “innovative, personalized therapies,” says Clive Svendsen, Ph.D., director of the Cedars-Sinai Regenerative Medicine Institute in Los Angeles. But he cautions that a great deal of work needs to be done before these cells can be transplanted into the brains of people with PD to treat the disease. One key question is whether the lab-engineered dopamine neurons would communicate like natural neurons in the brain. In theory, if the engineered replacement brain cells behaved like natural neurons, they could restore nearly normal movement for years.

ROLE OF PATIENTS AND ADVOCATES

A number of patients and patient advocates spoke at the NINDS conference. Jean Burns, an artist who has participated in 10 clinical trials and co-founded PDPlan4Life.com as a resource for patients, urges people with PD to enroll in clinical research trials. To scientists, she said, “I encourage you to use patients in your meetings; I hope you will remember me and remember to add the patient voice when you have your discussions.”

Linda Morgan, who also has PD, supports participating in clinical research trials and including patients and advocates in the research planning process. She urges scientists to balance their efforts on “long-game research” aimed at a cure for the disease with “short-game research” aimed at helping patients with their symptoms, especially fatigue.

Like Burns and Morgan, advocate Steven DeWitte has PD. He is another strong proponent of participating in clinical research trials. DeWitte started the Clinical Trial Transportation Program by partnering with Beth Israel Deaconess Medical Center in Boston, MA, to help volunteers with PD who lacked transportation participate in research studies. DeWitte participates in a program of the Parkinson’s Disease Foundation called Parkinson’s Advocates in Research (PAIR). For information on help with transportation needs and other support, go to pdf.org.

Daniel M. Lewis, who has had PD for 20 years and served as chairperson of the Parkinson Foundation of the National Capi-

AMERICAN BRAIN FOUNDATION EVENT

FREE Brain Health Fair Coming to Philadelphia!

Patients, families, and caregivers affected by neurologic conditions such as Alzheimer’s disease, stroke, Parkinson’s disease, traumatic brain injury, epilepsy, headache, multiple sclerosis, peripheral neuropathy—and many others—are invited to register now to attend the free Brain Health Fair. The event will take place on Saturday, April 26, 2014, from 10:00 a.m. to 4:00 p.m. at the Pennsylvania Convention Center in Philadelphia, PA. Registration is open to anyone interested in brain health at BrainHealthFair.com.

The Brain Health Fair is presented by the American Brain Foundation, the foundation for the American Academy of Neurology (AAN), which is bringing more than 12,000 neurologists and health-care professionals to Philadelphia for its Annual Meeting, the world’s largest gathering of neurologists.



“This is truly a once in a lifetime opportunity for the Philadelphia community to learn from some of the best and brightest neurologists in the world. They will teach free classes and share the latest advances in the prevention and treatment of brain diseases as well as ways for people to maintain a healthy brain,” says AAN member Brenda Banwell, M.D., chief, division of neurology, Children’s Hospital of Philadelphia.

The Brain Health Fair also features an exhibit hall, activities for kids and teens, musical performances, cooking demonstrations, giveaways, support groups, and celebrity appearances by former NFL star Ben Utecht and musician Billy McLaughlin.

For more information and to register for free, visit BrainHealthFair.com.

tal Area, stresses the importance of support groups and exercise for those living with a diagnosis of the disease. In the absence of a cure, it’s important for everyone who has PD to find ways of improving his or her quality of life, Lewis says. He notes that exercise provided “a dramatic change” for the better in terms of his own health.

Amy Comstock Rick, J.D., CEO of the Parkinson’s Action Network (parkinsonsaction.org), says everyone with a stake in PD research, including patients and advocates, should have a voice in the research agenda. “No research is successful in isolation,” she notes, adding that recommendations coming from the conference should reach as broad an audience as possible, including members of Congress.

To watch video interviews with experts in Parkinson’s disease, go to bit.ly/1fyjx2U.

FOR MORE INFORMATION

- ▶ For more *Neurology Now* articles on PD, go to bit.ly/1j50Mnz
- ▶ For articles on PD from *Neurology Today*, go to bit.ly/1gqRIZW
- ▶ To read Patient Pages on Parkinson’s disease (and other conditions) from *Neurology*, one of the American Academy of Neurology’s medical journals, go to bit.ly/1eAj5oY