

NARCOMS

WINTER 2014

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NOW

Vol. 3, Issue 1



SEEING DOUBLE:
MANAGING DIZZINESS & INFECTIONS

Congratulations to Steve W., Schaumburg, IL *NARCOMS Now Photo Contest Winter 2014 Winner*



“Hiking the Wave”

“This photo shows me engaging in two of my most rewarding activities: hiking and photography. It was taken in an area of the Paria Canyon-Vermilion Cliffs Wilderness [in Northeast Arizona, Southern Utah] called the Wave. Hiking to remote and unique places keeps me motivated to remain active and strong, and photography exercises my creative side and keeps my mind sharp. Staying physically and mentally active are valuable tools in fighting my MS.”

—Steve W.

A project of the Consortium of Multiple Sclerosis Centers



THE CONSORTIUM OF
MULTIPLE SCLEROSIS CENTERS

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NARCOMS NOW

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A Letter from the Director - Winter 2014

Hello,

Welcome to the Winter 2014 issue of *NARCOMS Now*.

All of us at NARCOMS wish you and yours a happy new year. In 2013 NARCOMS reached new milestones in overall enrollment, with more than 1,000 new participants for the year. We also have nearly 150 Twitter followers @NARCOMS. We'd like to thank you for your participation in NARCOMS. Whether you're new to the Registry or have been involved with us for years, we appreciate your taking the time to tell us about your life with MS.

In this, our eighth edition of *NARCOMS Now*, Dr. Avindra Nath, clinical director of the National Institute of Neurological Disorders and Stroke (NINDS) at the National Institutes of Health, discusses the risk of infections that can result from taking immunotherapies—common treatments for MS. From chicken pox to progressive multifocal leukoencephalopathy (PML), it is important to recognize the risk of a secondary infection in persons taking immunotherapies.

This issue includes several articles highlighting research relating specifically to NARCOMS participants. Have you suffered from dizziness while living with your MS? In this issue's "MS Reflections," we address the frequency and impact of dizziness in MS as experienced by NARCOMS participants. In "Snapshot" we review the number of scientific publications in the past year, many in prominent research journals, based on research from NARCOMS data.

"MS News" features research publications on the natural history of MS symptoms in NARCOMS participants, including a set of tables outlining the frequency of various MS symptoms. These tables show the commonality and severity of many symptoms in NARCOMS participants: mobility, hand function, vision, fatigue, cognition, bowel/bladder function, sensory, spasticity, pain, depression, and tremor/coordination. The discovery of a rare bacterium—commonly found in dirt, but not in humans—that some researchers consider could be a link to the cause of MS, is also highlighted.

We were thrilled with the number and range of photos you submitted to our *NARCOMS Now* photo contest. The contest continues through 2014, so if you are interested, submit your "MS life" story in pictures. For details see "Messenger" on page 13.

We continue to strive to be responsive to your thoughts and ideas about how we can make NARCOMS better, and so truly value your feedback. We look forward to engaging with you in the New Year, and thank you for your continued partnership with NARCOMS. We couldn't do it without you!



Dr. Robert Fox is the Managing Director of NARCOMS, the Medical Director at the Mellen Center for Multiple Sclerosis and a practicing neurologist at the Cleveland Clinic in Ohio.

Sincerely,

A handwritten signature in black ink that reads "Robert J. Fox". The signature is written in a cursive, flowing style.

NARCOMS INFORMATION CORNER



HAVE AN IDEA?

We would love to hear from you!
Send us your questions,
comments & suggestions.

Call: **1-800-253-7884** (toll-free US)

Email: narcomsnow@narcoms.org
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Who you'll hear on the phone:
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NARCOMS PROMISE

Your personal information is
always confidential.

The NARCOMS Global MS Patient Registry facilitates multi-center research on multiple sclerosis, developing collaboration between MS centers of excellence throughout the world to increase knowledge, improve clinical care, and enhance the quality of life for persons with MS.



VIEW PAST SURVEYS

www.narcoms.org

Click on: Participant Log in Here

Enter your username and password.
Select the correct picture, click Login.
Click the Form Summary link.

Choose the survey you would like to view from the drop down menus and click the **View Summary** link.
Print like you would any document.



EN ESPAÑOL

Para acceder a nuestro sistema a línea:

www.narcoms.org/es
Nuestro sitio de web es de alto seguridad a para su confidencialidad.

Para solicitar la envía de un cuestionario de inscripción por correo, llame al Registro NARCOMS al (800) 253-7884.



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Reminder when Completing Paper Surveys:

Please use pen rather than pencil when filling out NARCOMS paper surveys. Responses are scanned to electronic files for data capture and pen is easier to read. Thanks!

IMMUNOTHERAPIES AND RISK OF INFECTION:

An Interview with

Avindra Nath, MD, Intramural Clinical Director, NINDS

Dr. Avindra “Avi” Nath is a physician-scientist who specializes in neuroimmunology. Nath is the intramural clinical director of the National Institute of Neurological Disorders and Stroke (NINDS) [www.ninds.nih.gov] at the National Institutes of Health (NIH) [www.nih.gov]. At the 2013 Consortium of Multiple Sclerosis Centers/ACTRIMS conference, in Orlando, Florida, Nath presented a talk on “Infectious Complications for Immunotherapies in MS” aimed at raising doctors’ and patients’ awareness of the risk of infections with MS. He spoke with NARCOMS Now about infections that can be caused by immunotherapies taken to treat multiple sclerosis, and the need for increased awareness about their risk.

MS patients are likely familiar with immunotherapies, which are commonly used to treat the disease. An immunotherapy can be defined as a disease treatment that works by kick starting, enhancing, or weakening an immune response. In other words, it acts as the fuel to start your body’s fight against a disease. There are two types of immunotherapies, identified as **activation immunotherapies**, those that stimulate the immune system to destroy diseased cells; and **suppression immunotherapies**, which reduce an abnormal immune response. The active agents of immunotherapies are called, collectively, immunomodulators.

You may have heard of **interferons**, which are the immunomodulators most commonly used to treat MS. Interferons are

proteins made by host cells when those cells are infected with viruses, bacteria, parasites, or tumor cells. The interferons allow the cells to talk and trigger the immune system’s protective defenses, to fight off the intruders.

Dr. Avindra Nath has spent many years studying the relationship between the use of immunotherapies to treat long-term illnesses such as MS, and the infections that can result from the use of these therapies. He began his research in this area looking at the AIDS virus during the AIDS epidemic, in the 1980s. Nath studied the effects of secondary infections, such as progressive multifocal leukoencephalopathy (PML) and the herpes viruses, on HIV patients. He is now conducting research on MS patients with similar infections.

Immunotherapies and Risk of Infection

“With MS, suppressing the immune system is very effective in treating the disease, but then you see infections,” Nath says about some MS therapies. “The pattern and type of those infections is similar to the types of secondary infections we see in patients with AIDS.”

PML is one such rare infection, which can be caused by taking natalizumab (also known by its brand name, Tysabri) for relapsing MS. PML is a brain infection that can cause paralysis and even death, and there is no known cure.

“PML is caused by a DNA virus called JC virus—most of us are infected with it in childhood but our immune system keeps it at bay,” he says. The virus can be reactivated, and it may then affect the brain. It grows in the brain’s glial cells, and then gradually spreads from cell to cell in the brain. Untreated, it can go from onset of symptoms to death within six months, although most MS patients with PML taking natalizumab survive.

Currently there is no antiviral drug available to treat infections like PML. The only treatment is to reverse the body’s immune-deficient state by using plasma exchange to accelerate the removal of the drugs that put patients at risk of PML in the first place. But researchers like Nath are working on developing a drug that directly targets the virus to treat this infection.

“We have a large drug discovery effort underway and some good candidates have been identified which we want to take forward,” Nath says. These ongoing studies are still in the lab, and have not yet been introduced into animals—a requirement

for the FDA to move testing into human subjects. The NIH does have a clinical study for PML that is currently enrolling patients. [<http://goo.gl/8BJhJq>]

Nath encourages researchers to look beyond the boundaries of a single disease they may have studied throughout their career, to see how it may be similar to other illnesses.

“What we’ve learned by studying human diseases is that information about one disease can actually translate to another,” Nath says. “Research in AIDS can be beneficial to MS patients. Those things can be hard to anticipate but the reality is we’re often stuck in the idea that ‘I need to support my disease.’ We as researchers need to think beyond those boundaries.”



Another class of infections that can affect MS patients on immune suppressive therapies is the herpes virus, of which there are many different types. The virus that causes oral herpes, herpes virus type 1, can sometimes affect the brain and cause encephalitis, or acute swelling. The chicken pox virus is another herpes virus, called varicella zoster virus, which can develop into shingles, and in some patients invade the brain and other organs. However, these infections are still very rare in MS patients. As opposed to PML, effective antiviral drugs are available for treating herpes infections, so early recognition and treatment are necessary.

Even if MS patients are not taking immunosuppressants they often still get infections of the bladder, or lung, for example, and then those can spread. Normally T cells suppress these types of infections, but once these cells are not effective as might be the case in patients on immune suppressive therapy, the infections are ready to emerge. For PML, the JC virus is resident in the bone marrow, spleen and kidneys. Once the immune system is suppressed, these viruses have to change genetically to invade the brain.

“Early diagnosis is key because here we do have effective treatments,” Nath says. “The key is to diagnose these infections within a day or less, particularly for encephalitis caused by herpes viruses which can be much more rapid to develop than PML.” And MS patients should not assume that because they had a vaccine against shingles, for example, they won’t

be affected by it. This is because vaccines work by boosting the immune system, but some immune suppressive drugs would override these effects. “If your immune system is compromised, there is a chance the vaccine isn’t going to do much for you, so you’re still at risk.”

Nath points out that currently, some “MS doctors are not familiar with these infections—although most AIDS doctors are. They can present in very strange, non-classical forms because of the immune suppression,” he says. Sometimes early symptoms of infections can be mistaken for MS symptoms.

“Early diagnosis [of secondary infections] is key because we do have effective treatments.”

“Meanwhile the patient gets worse and by then you’ve lost precious time,” Nath says. “I want to make sure MS neurologists recognize these infections,” Nath says. “You cannot separate the immune system and infections.

“Our goal is to train a new cadre of neurologists who understand infections. I think people will be surprised to see how difficult it can be sometimes to diagnose these infections and that they are also complicated to treat.” Nath encourages MS doctors who see symptoms or issues with which they are not familiar to contact the National Institutes of Health. [www.nih.gov]

Immunotherapies and Risk of Infection

The last 20 years have shown great advances in the study and treatment of MS, Nath says, “more than in any other neurological disease.” Prior to that, many drugs were tested to treat MS but many failed, repeatedly. Clinical trials in MS initially focused on progressive MS because the clinical course was considered more “predictable” than relapsing remitting MS, in which it would be difficult to show a breakthrough because it comes and goes and thus has an unpredictable course, Nath says. Unfortunately, all those clinical trials failed. The application of MRI to MS was a huge advancement to the development of treatments for MS, Nath says, [for more on the introduction and use of MRI treatments for MS, see the Spring 2013 article, “Why MRI?”], and then the research focus changed to relapsing remitting MS because MRI allowed researchers to quantify the lesions in the brain over a period of time. Thus the effects of drugs on the accumulation of these lesions could be determined.

“If you have a drug that makes a little bit of difference, that’s still a huge advancement to the field when before that you had nothing, because if we can understand the mechanism by which the drug works we can improve upon it,” Nath says. “MS is a perfect example—we keep coming up with better and better ways to treat it. And MS has also benefited from the development of drugs to treat arthritis and lupus. However with some of these drugs such as inhibitors of tumor necrosis factor, unexpected side effects occurred in MS patients. So again, every time you modify the immune system you have to be very careful.”

What Nath would like MS patients to know is that if there is a change in their health status while they are on immune suppressive therapies they should report it to their doctor. “Weakness, cognitive abnormality, trouble remembering—don’t delay in reporting it. They should keep up with their flu and other vaccines and also report and treat aggressively any lung or bladder infections.”

“If we can understand the mechanism by which a drug works, we can improve upon it. MS is a perfect example—we keep coming up with better and better ways to treat it.”

While major advancements have occurred in our ability to treat MS patients and alter the course of the illness, much more research is necessary to mitigate the risks associated with such therapies. Many of these advancements are likely to come from studying patients with other diseases who are also vulnerable to such infections. This requires interdisciplinary research and a strong partnership between academia including the National Institutes of Health, industry, and private foundations, since each of these organizations have unique strengths and resources and share the common goal of improving the lives of patients with MS.



Q: Why wasn't my MS medication, Tecfidera®, listed in the spring update survey?

A: Tecfidera® is the registered commercial (brand) name for the oral medication dimethyl fumarate (also known as BG-12). During the drug's clinical trial period from 2009 to 2013, NARCOMS update surveys listed the drug under those generic names. The FDA approval of dimethyl fumarate (along with its trade name designation, Tecfidera) occurred after NARCOMS finalized production of the spring 2013 update.

In the fall 2013 update survey Dimethyl Fumarate (Tecfidera®, BG-12) appears in the same format as all the other medications: listed by the generic name followed by the brand name, with any other common or commercial names in parentheses. As other new medications and brand names become approved for treatment of MS, they will be added to the list .

If you have any questions about matching the medication you are taking with those listed in a NARCOMS update, please call us and we will be happy to assist you: 1-800-253-7884 (toll free US). For more information on MS medications, please see "NARCOMS Messenger" on page 13.

Q: Why do you continue to ask relapse questions in every survey when not everyone has Relapsing MS? Why should I answer them if I have progressive MS and my symptoms haven't changed?

A: Approximately 80% of persons diagnosed with MS are first diagnosed with a relapsing form of MS. Over time, people with relapsing forms may transition to progressive MS. Although clinical relapses are uncommon after transitioning to progressive MS, they can still happen. To more accurately describe changes in MS over time, it is important to continue to capture all participants' relapse information.

If you are no longer experiencing relapses, simply answer "No" to that question and move on. Even if you are answering "No Change" or your symptoms have remained stable, this information helps to describe the pattern of MS symptoms across the whole spectrum of MS and its disease course.

To submit a question for Q&A please email narcomsnow@narcoms.org

SURVEY 101

PAPER OR ONLINE SURVEYS: WHAT IS THE DIFFERENCE?

As you know, NARCOMS update surveys are available in both paper and online versions. Approximately 30% of the NARCOMS participants receive their survey in the mail to complete on paper and then send back to the NARCOMS coordinating center. You may have wondered what is the difference between the versions? When it comes to the update questions – nothing! The questions we ask for paper and online are exactly the same and have exactly the same answer options.

THERE ARE A FEW DIFFERENCES IN THE WAY THE SURVEY IS COMPLETED:

SIGNATURES:

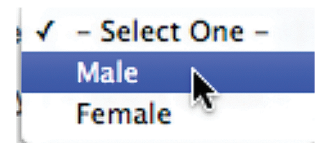
- Paper participants must sign their paper update – if you leave off the signature, someone from NARCOMS will contact you to make sure we can use your responses.
- Since the online participants can't sign their forms, they are asked to agree to their data being used.

ANSWER SELECTIONS:

- Online participants will usually have what is called a “dropdown” list to select an answer for questions where only one answer is allowed.
- Paper participants can see all the options on the paper version but should still only select one answer where indicated. Checking more than one answer on the paper questions that ask you to only select a single answer can cause delays in the use of your data, and may result in your response not being used for research.

Otherwise, the responses for all surveys are kept in the same data files and used in the same way for research. If you have any questions about how the surveys are completed, please give us a call!

Online Dropdown:



Paper Question:

- Gender (Select One):
- Male
 - Female

Have an idea for Survey 101?

If you have any questions about how these updated survey questions apply to you, don't hesitate to call us at 1-800-253-7884.

THE FREQUENCY AND IMPACT OF DIZZINESS IN THE NARCOMS POPULATION

Ruth Ann Marrie, MD, PhD

Departments of Internal Medicine and Community Health Sciences, University of Manitoba, Winnipeg, CAN

INTRODUCTION

Dizziness is a common symptom, and affects almost one-quarter of the general population (23%).^{1,2} Dizziness is a term that can mean faintness, lightheadedness, a feeling of imbalance or vertigo. Vertigo is characterized by the false impression of movement when no movement is present. For example, one might feel that the room is spinning while standing still. Dizziness is also common in persons with multiple sclerosis (MS), affecting up to 59% of persons with MS.³⁻⁵ Vertigo may be the first symptom of MS in up to 5% of persons,⁶ yet very few studies have looked at how dizziness affects the lives of persons with MS.

THE QUESTIONS

In the Spring 2004 update questionnaire we asked NARCOMS participants to fill out the Dizziness Handicap Inventory (DHI).⁷ The DHI is made up of 25 questions that aim to assess the impact of dizziness. It was created to help health care providers determine how well patients responded to treatment of dizziness. The questions ask about the activities that make dizziness worse, such as turning over in bed or looking up. The questions also ask about how people feel about their dizziness, including how it affects their mood. Finally, the questions ask about how the dizziness may limit a person's activities. Each question can be answered as 'yes' (4 points), 'sometimes' (2 points) or 'no' (0 points). Responses to the questions are added up to get a total score. The lowest score is 0 which means no handicap related to dizziness.

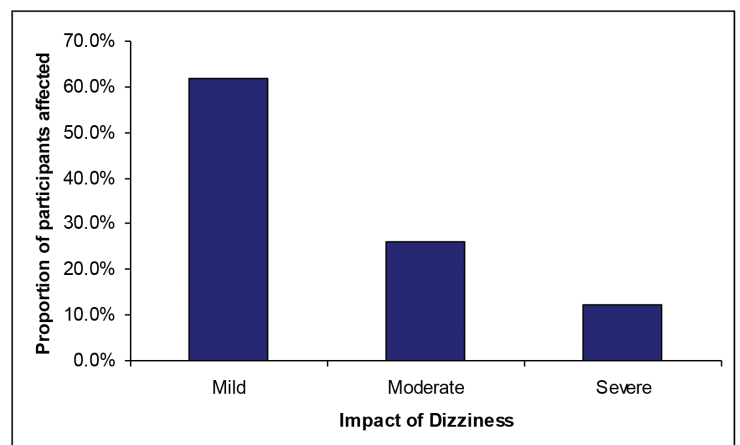
The highest score is 100. Other researchers have suggested that the total scores be grouped as mild (0–30 points), moderate (31–60 points), and severe (61–100 points).⁸ Along with the DHI we asked participants to fill out the Short Form-12 (SF-12) questionnaire, used to measure health-related quality of life.

STUDY PARTICIPANTS

A total of 8,123 NARCOMS participants were included in the study.⁹ Of these 25% were men and 75% were women. Ninety-six percent were white, while 3.8% reported another race. Their average age was 58.0 years.

DIZZINESS

The median total score on the DHI was 20. Of 8,123 participants, 1984 (26.2%) reported scores of zero, indicating that they did not have any concerns related to dizziness. This means that 73.8% of participants reported at least some dizziness. The impact of dizziness was mild in more than 60% of participants, moderate in 25.9% and severe in 12.3% (Figure 1).



Respondents most commonly answered “yes” or “sometimes” to those questions relating to symptom worsening with head movements (56.0%), bending over (54.5%), and looking up (47.5%) (Table 1).

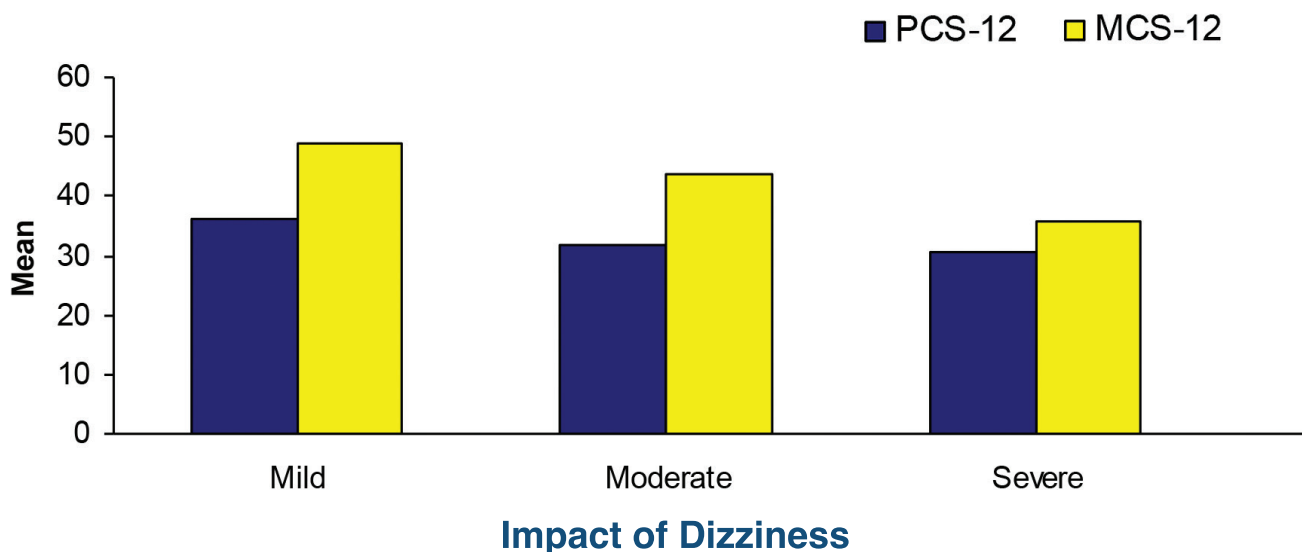
Table 1. Responses to the Dizziness Handicap Inventory in the NARCOMS population

<u>Dizziness Handicap Inventory</u>	Yes or Sometimes (%)	No (%)
Does looking up increase your problem?	47.5	52.5
Does walking down the aisle of a supermarket increase your problem?	27.5	72.5
Does performing more ambitious activities like sports, dancing, household chores such as sweeping or putting dishes away increase your problem?	46.0	54.0
Do quick movements of your head increase your problem?	56.0	44.0
Does turning over in bed increase your problem?	19.4	80.6
Does walking down a sidewalk increase your problem?	29.9	70.1
Does bending over increase your problem?	54.4	45.5
Because of your problem, do you restrict your travel for business or recreation?	27.4	72.6
Because of your problem, do you have difficulty getting into or out of bed?	27.7	72.3
Does your problem significantly restrict your participation in social activities such as going out to dinner, going to movies, dancing, or to parties?	29.4	70.6
Because of your problem, do you have difficulty reading?	32.4	67.6
Because of your problem, do you avoid heights?	38.6	61.4
Because of your problem, is it difficult for you to do strenuous housework or yard work?	46.9	53.1
Because of your problem, is it difficult for you to go for a walk by yourself?	38.9	61.1
Because of your problem, is it difficult for you to go for a walk around your house in the dark?	41.8	58.2
Does your problem interfere with your job or household responsibilities?	41.4	58.6
Because of your problem, are you afraid people may think you are intoxicated?	32.8	67.2
Because of your problem, do you feel frustrated?	42.7	57.3
Because of your problem, are you afraid to leave home without having someone with you?	21.2	78.8
Because of your problem, have you been embarrassed in front of others?	23.8	76.2
Because of your problem, is it difficult for you to concentrate?	38.4	61.6
Because of your problem, are you afraid to stay home alone?	7.52	92.5
Because of your problem, do you feel handicapped?	33.6	66.4
Has your problem placed stress on your relationship with members of your family or friends?	24.3	75.7
Because of your problem, are you depressed?	30.1	69.9

MS REFLECTIONS

Persons who reported a higher impact of dizziness on the DHI reported both lower physical and mental qualities of life (Figure 2).

Effect of dizziness on physical (PCS-12) & mental (MCS-12) quality of life



SUMMARY

Dizziness is common in persons with MS. And dizziness has a negative impact on daily activities and quality of life. Given the impact of dizziness on persons with MS, more research about dizziness and its treatment is needed.

DEALING WITH DIZZINESS

Dizziness is a common symptom of MS, and in fact is often one of the first symptoms people notice. People with MS may feel off balance or lightheaded. Much less often, they have the sensation that they or their surroundings are spinning—a condition known as vertigo.

These symptoms are due to lesions—damaged areas—in the complex pathways that coordinate visual, spatial, and other input to the brain needed to produce and maintain equilibrium, according to the National Multiple Sclerosis Society. They suggest

consulting a physician when dizziness or vertigo becomes bothersome or lasts a long time. Usually, dizziness can be treated with anti motion-sickness drugs such as meclizine (Antivert[®], Bonine[®], or Dramamine[®]), skin patches that deliver scopolamine, or the anti-nausea drug ondansetron (Zofran[®]). In very severe cases of dizziness or vertigo, a short course of corticosteroids can be administered.

As with any symptom, if you are experiencing dizziness, speak with your doctor or care provider to learn about ways to treat it.

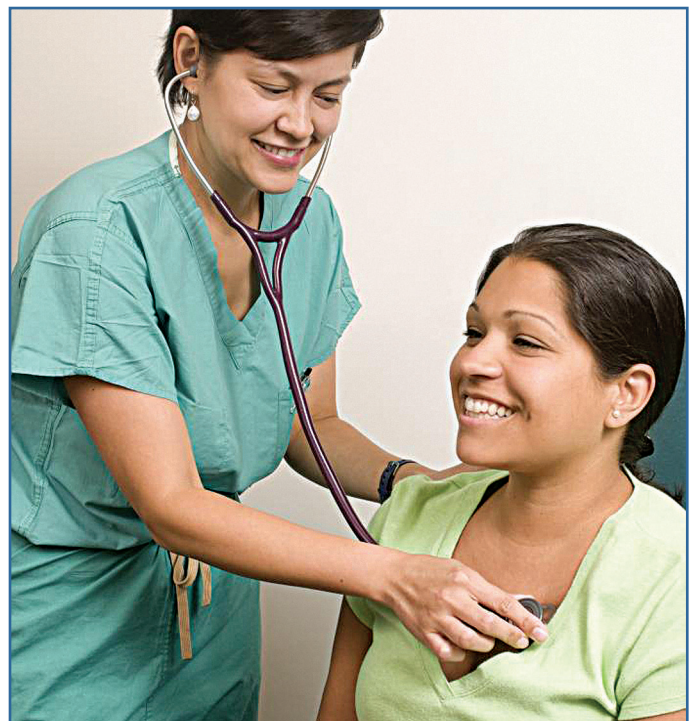
MSAA Expands its MS Research Update

In spring 2013 the **Multiple Sclerosis Association of America** for the first time published an expanded update to its *MS Research Update* (published in prior years in *The Motivator*, the organization's magazine). The publication serves as a comprehensive overview of research findings on the FDA-approved disease-modifying therapies, as well as many experimental treatments. The publication is broken into three main categories, covering "FDA-Approved Medications," "Experimental Medications," and "New Directions in MS Research." The "Update" includes such useful information as an explanation of the trial phases for investigating drugs and treatments. You can read the entire update online at: mymsaa.org/ms-research-update. The publication is available for download as a PDF, or you can order it online to be shipped to you.

Affordable Care Act Info Site Specific to MS

We tip our hat again to the MSAA with their valuable new online resource in teaching about the Affordable Care Act and how it will affect those living with MS. The organization has created a comprehensive section on its website dedicated to the topic, at mymsaa.org/aca. Located under the "About MS" tab, the ACA "Changes in Insurance" section offers: webinars on ACA, sections on changes in Medicare and changes in non-Medicare insurance, as well as a link to a brochure on "*The Affordable Care Act and Multiple Sclerosis*."

Open enrollment for insurance coverage through the Marketplaces began October 1, 2013, with policies taking effect January 2014. Note: MSAA has been approved as a Champion of Coverage to partner [<http://goo.gl/QRY0kJ>] with the Centers for Medicare and Medicaid Services to spread awareness of and encourage enrollment in the ACA Marketplace.



NARCOMS Now Photo Contest

Thank you to everyone who submitted all your fantastic photos for our "Living with MS" contest! You'll see this issue's contest winner featured in the inside front cover of the magazine. The contest continues online, where you can vote for a winner and submit a photo of your own. Visit www.narcoms.org/narcomsnow/photocontest for guidelines, and feel free to email us your entry at: narcomsnow@narcoms.org.

NARCOMS Researchers Publish on “Natural History of Multiple Sclerosis Symptoms” in Fall 2013 *International Journal of MS Care*

Using data provided by NARCOMS participants in our surveys, a group of researchers published the results of a study on the history of MS symptoms in the latest issue of the *International Journal of MS Care*, an open-source journal published quarterly by the Consortium of Multiple Sclerosis Centers (CMSC).

The NARCOMS database contains information from more than 35,000 patient volunteers on the severity of symptoms in 11 areas commonly affected in MS: mobility, hand function, vision, fatigue, cognition, bowel/bladder function, sensory, spasticity, pain, depression, and tremor/coordination.

The study set out to calculate the frequency of each of these symptoms in the first 30 years they appear. A resulting set of “symptom frequency tables” show that most participants note that within the first year of having the disease, they show some degree of impairment, in most areas. Impairment in all areas becomes more severe the longer a patient has the disease, but not all at the same time, nor at the same levels. Sensory symptoms (numbness, tightness, tingling, or burning) and fatigue were especially common: within the first year after disease onset, 85% of patients reported some degree of sensory symptoms and 81% some degree of unexplained

fatigue. Half of the patients (50%) noted minimal or mild cognitive impairment within the first year.

Mobility, generally thought to be unaffected in the first decade of disease, was reported here as “noticeably affected” in 35% of patients in the first year; an additional 15% had at least an occasional need for a mobility device, such as a cane or walker.

The symptom frequency tables illustrate the magnitude of a patient’s perceived impact of the disease, and highlight the extent of unmet need in symptomatic management. The tables are easy to use and allow MS patients and their clinicians to compare an individual’s own impairment in any of the 11 domains to that of NARCOMS participants with the same disease duration. The tables are available to view online at: <http://goo.gl/TFPOvV>.

Study Suggests A Rare Bacterium Found in Soil Could Be Missing Link in MS Cause

In a story that made its way to *Newsweek* magazine in October 2013, a research team from Weill Cornell Medical College and The Rockefeller University (both in New York City) has identified a bacterium it believes may trigger multiple sclerosis (MS).

The study, published in *PLoS ONE*, is the first to identify the bacterium, *Clostridium* (C.) *perfringens* type B, in humans. It is normally found in grazing animals such as cows and sheep.

The study describes discovery of *C. perfringens* type B in a 21-year-old woman who was experiencing an MS flare. The woman was part of the Harboring the Initial Trigger for MS (HITMS) observational trial launched by Dr. Timothy Vartanian, professor of neurology and neuroscience at Weill Cornell Medical College and director of the Judith Jaffe Multiple Sclerosis Center at New York-Presbyterian Hospital/Weill Cornell Medical Center, and K. Rashid Rumah, an MD/PhD student at Weill Cornell Medical College.

C. perfringens types B and D carry a gene (epsilon toxin) that emits a protoxin—a non-active precursor form of the toxin—which turns into the potent “epsilon” toxin in the intestines of grazing animals. The epsilon toxin travels through the blood to the brain, where it damages brain blood vessels and myelin, the insulation protecting neurons, resulting in MS-like symptoms in the animals. While the D subtype has only been found in two people, the B subtype had never been found in humans.

While the scientists acknowledge their study is small and must be expanded before a definitive connection can be made between the pathogen and MS, the findings are so intriguing they say they have already begun working on new treatments for the disease.

“That we identified this bacterium in a human is important enough, but the fact that it is present in MS patients is truly significant because the toxin targets the exact tissues

damaged during the acute MS disease process,” say the study’s first author, Rumah.

“While it is clear that new MS disease activity requires an environmental trigger, the identity of this trigger has eluded the MS scientific community for decades,” Vartanian says. “Work is underway to test our hypothesis that the environmental trigger for MS lays within the microbiome, the ecosystem of bacteria that populates the gastrointestinal tract and other body habitats of MS patients.”

Examining Potential Risks and Treatments

Vartanian says researchers do not know how humans are infected with *C. perfringens* type B or D, but they are studying potential routes of exposure. The scientists are also in the first stages of investigating potential treatments against the pathogen.

A vaccine is one possibility—one exists for farm animals, but requires repeat immunizations. “We are also investigating the possibility of developing small-molecule drugs that prevent the toxin from binding to its receptor,” says Vartanian.

A favorite approach, Vartanian says, is the development of a probiotic cocktail to deliver bacteria to compete with and destroy *C. perfringens* types B and D. “It would be such a beautiful and natural way to treat the gastrointestinal system and solve the problem. We are also starting to work on this approach.”

Using Latest Technologies to Help Track MS Symptoms

PCORI Pilot Program Supports Use of Tablets to Track Symptoms

Multiple sclerosis is a disease that can have a vast variety of symptoms and require multiple types of treatments over its duration. A team of MS experts in California devised a digital “portal” to predict disease course and guide medication choices.

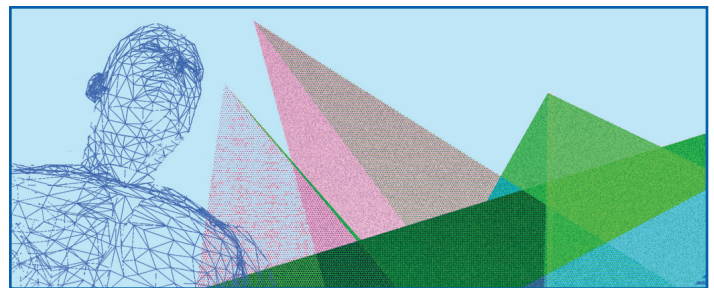
Using tablet computers, researchers based at the (UCSF) School of Medicine converted a program called **BioScreen**—into an accessible information source for patients to use with guidance from their clinicians.

Over the past decade, a research team led by Stephen Hauser, MD, Chair of Neurology at UCSF, has collected mass quantities of data from 800 MS patients, following each for more than eight years. A patient’s entry in BioScreen includes brain-imaging, genetic, physiological, blood-chemistry, and environmental-exposure data. It also describes the disease course and treatment. BioScreen allows patients to visualize the data, compare individual profiles to those and guide the choice of treatment of other patients with similar characteristics.

BioScreen was originally designed for researchers and physicians. But with the **Patient-Centered Outcomes Research Institute (PCORI)** Pilot Project funding, the UCSF team is converting the tool into an accessible source of information for patients to use with guidance from their clinicians. Patients using the tool are helping

to guide BioScreen’s future development. A dozen or so patient partners have indicated which treatment factors are most important to them, such as the frequency at which they need to take their drugs. The project’s eventual goal, the researchers say, is to make predictions about the evolution of a patient’s disease.

MS patients and their clinicians need medical information presented in a coherent, organized fashion to make better-informed decisions. “With BioScreen, we can say ‘We have five possibilities for picking a drug for you. Let’s look at patients who two years ago were at the same stage as you now.’ Your personal decision is now informed by real data,” says Pierre-Antoine Gourraud, PhD, MPH, researcher in a group led by Hauser. “The more patients we add to the BioScreen, the more this evidence base will grow—and the more accurately we can predict the future of every patient.”



“With a chronic and complex disease like MS, there are very personal treatment decisions that must be made by patients,” Hauser observes. “They may think to themselves, ‘How do I feel about the unlikely, yet not impossible, event of a life-threatening side effect of this medicine?’ The BioScreen provides an evidence basis for the range of possible options so that patients can make the most informed decisions possible.”

**Time on 25-foot Walk Performance Test
“Determines How MS Affects Patients”**

Doctors may be able to determine the progression and severity of multiple sclerosis in a patient by measuring the time it takes him to walk 25 feet, according to a study published in the journal *Neurology*.

The “25-foot walk performance” is used to determine the level of disability in a person suffering from MS; researchers say these findings show that the time it takes for a patient to walk this distance may be an indicator of disease progression and severity.

For the study, the researchers analyzed 159 patients with MS who were asked to carry out a timed 25-foot walk. Patients were also asked about their employment, and daily activities, and if they used assistance when walking.

A second group of 95 patients with MS was used to confirm the team’s results.

The researchers found that patients who took longer than 6 seconds to walk 25 feet were more likely to be unemployed, have a change in occupation as a result of the disorder, use a cane for walking, and require help with day-to-day activities, such as house cleaning and cooking.

The participants who took 8 seconds or longer to walk 25 feet were more likely to be unemployed, divorced, require a walker for mobility, and use Medicaid or Medicare. They were also 70% more likely to be unable to carry out day-to-day activities, such as grocery shopping, house cleaning, laundry and cooking.

Myla Goldman, MD, Neurologist at the University of West Virginia in Charlottesville, says these findings could be useful in providing “benchmarks” in the progression of MS.



“We already know that the timed 25-foot walk test is a meaningful way to measure disability in MS,” Goldman says. “Our study builds on that research by providing a clearer idea of how walk time can provide information about how a person’s disease progression and disability impacts their everyday activities and real-world function. Based on these findings, we propose that a timed 25-foot walk performance of 6 seconds or more, and 8 seconds or more represent meaningful benchmarks of MS progression.”

The researchers note that although their findings were confirmed in two groups of patients with MS, further research is needed with “larger longitudinal studies across the entire performance of the times 25-foot walk continuum ... to expand our understanding of the clinical meaningfulness of observed changes in this very important MS outcome.”

2013 Roundup: NARCOMS Data in Publication

In 2013, a record number of 18 research articles were published in peer-reviewed journals utilizing information many of you have provided in NARCOMS update and supplementary surveys. The topics include reproductive and sexual health (1-5), vision and cognition (6-8), mobility and disability (9-11), natural history of MS among NARCOMS participants (12), relapses (13), quality of life in MS (14-17), and sources of health information used by NARCOMS participants (18). These articles will help to inform the MS community at large, including healthcare providers and doctors who treat people living with MS, about the changes in MS associated with specific conditions and over time.

Here is the listing of the articles, by title, with the journal that published the research and a link to a website where the summary of results or the entire article can be found:

1. Multiple sclerosis and pregnancy: a comparison study. *Canadian Journal of Neurological Science*: <http://goo.gl/RgNgYc>
2. Reproductive decision making after the diagnosis of multiple sclerosis (MS). *Multiple Sclerosis*: <http://goo.gl/Jo9Fck>
3. Sexual dysfunction in patients with multiple sclerosis. *Multiple Sclerosis and Related Disorders*: <http://goo.gl/MjD4WP>
4. The impact of sexual dysfunction on health-related quality of life in people with multiple sclerosis. *Multiple Sclerosis*: <http://goo.gl/rli4nw>
5. The Multiple Sclerosis Intimacy and Sexuality Questionnaire -- re-validation and development of a 15-item version with a large US sample. *Multiple Sclerosis*: <http://goo.gl/IRpsYD>
6. "Seeing" in NARCOMS: a look at vision-related quality of life in the NARCOMS registry. *Multiple Sclerosis*: <http://goo.gl/4IITTG>
7. Cognitive reserve and symptom experience in multiple sclerosis: a buffer to disability progression over time? *Archives of Physical Medicine and Rehabilitation*: <http://goo.gl/gWkPaU>
8. Cognitive reserve and patient-reported outcomes in multiple sclerosis. *Multiple Sclerosis*: <http://goo.gl/EhkQdQ>

9. Impact of mobility impairment on indirect costs and health-related quality of life in multiple sclerosis. *PLoS One*: <http://goo.gl/MdrR54>
10. Mapping the 12-item multiple sclerosis walking scale to the EuroQol 5-dimension index measure in North American multiple sclerosis patients. *BMJ Open*: <http://goo.gl/Vg8j7C>
11. Disability in multiple sclerosis: a reference for patients and clinicians. *Neurology*: <http://goo.gl/wnIVYD>
12. Natural History of Multiple Sclerosis Symptoms. *International Journal of MS Care*: <http://goo.gl/b8hNKs> → See “MS News” for more on this research, page 14.
13. The multiple sclerosis relapse experience: patient-reported outcomes from the North American Research Committee on Multiple Sclerosis (NARCOMS) Registry. *BMC Neurology*: <http://goo.gl/xxcGWO>
14. Change in the Health-Related Quality of Life of Multiple Sclerosis Patients over 5 Years. *International Journal of MS Care*: <http://goo.gl/Hwi8Dr>
15. Specialized housing and transportation needs of adults with multiple sclerosis. *Work*: <http://goo.gl/mNcjdu>
16. The prevalence of urinary catheterization in women and men with multiple sclerosis. Reported in the *Journal of Spinal Cord Medicine*: <http://goo.gl/9aHQqx>
17. Substantial burden of dizziness in multiple sclerosis. *Multiple Sclerosis and Related Disorders*: <http://goo.gl/P453KW>
18. Preferred sources of health information in persons with multiple sclerosis: degree of trust and information sought. *Journal of Medical Internet Research*: <http://goo.gl/koWW2Y>

In addition to the published research, researchers gave more than 20 NARCOMS-related presentations at scientific meetings in the US and Europe, covering a broad range of NARCOMS-related topics. We look forward to continuing to report on MS-based research in 2014. None of this research would be possible without you, the NARCOMS participants, so thank you!



Scan QR code for links to articles mentioned in NARCOMS SnapShot.

play

Find the following hidden words:

resolve, hope, faith, strengthen, educate, learn,
evolve, work, inspire, understand, listen, explore,
overcome, accept, change, rewrite, transform, illuminate

Z	C	E	N	M	O	E	A	O	C	V	N	S	C	E	I	O	R
U	U	H	E	O	G	K	E	G	N	E	R	P	A	A	T	E	T
O	U	O	R	S	H	Q	E	F	E	H	L	S	T	F	G	S	Z
D	G	P	N	A	C	C	E	P	T	E	R	I	I	P	E	E	E
O	D	E	L	R	S	D	C	J	S	P	M	N	U	R	D	R	G
N	E	V	I	D	A	E	B	I	I	E	S	O	U	U	L	E	U
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FIND THE ANSWERS TO THIS WORD PUZZLE ONLINE:

www.narcoms.org/narcomsnow/play/answers

FACES OF NARCOMS

THANKSGIVING THOUGHTS ON MS

It was the year before our country would celebrate its 200th birthday—1975. While planning Thanksgiving dinner, my son and I talked of bicycling across the country for the celebration. He always enjoyed helping with holiday planning, and this year I was especially glad, as I became tired so quickly. I thought perhaps I needed more exercise so I went swimming, but after each swim I could hardly drag myself home, let alone plan a festive Thanksgiving.

I survived Thanksgiving, but realized something wasn't right. A few days later when I awoke, the vision in my left eye was cloudy. My husband made an appointment with our doctor. After a few simple tests the doctor sent me to an ophthalmologist. He called my condition "optic neuritis" and said perhaps it would go away with cortisone—or it might be MS.

I had only heard of the illness a year before, when a friend's neighbor had it—and it sounded scary. Of course I couldn't have it; I had too much going on in my life with 5 children and I had thrown myself into volunteer work. No, I couldn't have MS.

My doctor recommended seeing a neurologist. This appointment involved extensive testing of my eyes and balance. When the tests were done, the neurologist repeated what my doctor had said: This might clear up and I would be fine, it could be minor strokes or a demyelinating disease. None of these options sounded good, but we went home and tried to keep on with our lives as they had been. My vision cleared up, but then, almost monthly, other strange things happened: Half my head would have no feeling when I combed my hair or I was unable to hold a pen.

Every month we'd visit the neurologist and every time they'd say it might be MS, but we had to rule out everything else. The only way we could tell for sure was by eliminating what it wasn't.

A year later, I woke up and could not lift my head from the pillow, I was so dizzy. My husband made an appointment at the neurologist's office, which wound up being the first time "it" was called MS. Of course I knew they were wrong—I would be there a few days, have a nice rest, and go home. Instead, I was there three weeks, had daily physical therapy and was treated to hydrotherapy in 65-degree water, since they felt that cooling the body would lead to more rapid improvement.

That was half a lifetime ago. Since then, I have had few exacerbations, thanks in part to a positive outlook and deep spiritual resources. I've always seen the cup as half full, not half empty, an attitude I developed from my constant searching for higher spiritual values.

—Marti P.

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