Remyelination and Repair – Current Science Brings Hope for the Future

Written by Kyle Smoot, M.D., F.A.A.N.

Multiple Sclerosis (MS) is a disorder of the immune system. The immune system protects the human body from infections and the development of many diseases. However, in MS, a subset of cells get misguided, resulting in injury to parts of the brain, spinal cord and/or the optic nerves. This leads to a loss of the protective sheath, called myelin, and sometimes injury or destruction of the axon, which carries neurologic signals. The latter causes permanent neurologic symptoms and deficits.

Currently, we have an extensive number of disease modifying therapies (DMTs) for patients with relapsing MS and, more recently, a treatment (ocrelizumab) for patients with the progressive phase of the disease. The goal of DMTs is to prevent the disease from progressing; however, these medications do not repair the damage caused by MS. Therefore, symptoms such as weakness, sensory loss, and balance do not improve with DMTs.

MS research is trying to identify therapies which may help repair damage, specifically to the myelin. One possible example is opicapnumab (anti-LINGO). LINGO-1 is present in the brain and its function is to prevent re-myelination (repair of the nerve). This protein is part of a checks and balances system; however, LINGO-1 might be overactive in MS patients, preventing the oligodendrocytes from developing. These cells are important as they are responsible for making myelin. In an earlier phase of a clinical trial (Phase II), there were no safety issues identified with anti-LINGO, which is a monthly IV infusion. While there was no clinical improvement in vision, one test showed the amount of time for the electrical signal to travel from the eye to the brain improved, suggesting some repair. If the trial were conducted longer, some clinical improvement may have been noticed. A larger trial with more patients is currently underway, and Providence Multiple Sclerosis Center is one of the centers participating. The study has completed enrollment, so hopefully, we will have results in 2020.

In small studies, mostly conducted in France, high doses of Biotin (Vitamin H) have been reported to improve neurologic function in people with MS. Studies suggest biotin may help improve energy use within the axon and promote remyelination. A large clinical trial (Phase III) of Biotin in 600 patients worldwide with progressive MS has completed enrollment. Results will be available later this year.

Another Phase II clinical trial, which will soon be enrolling at Providence MS Center, is evaluating a relatively new therapy called elezumab. This trial will be open to patients with relapsing and progressive phases of MS. Elezumab is an IV infusion given every 4 weeks for about a year. This therapy targets repulsive...
How long have you been at Providence?
Just 3 months so far! And looking forward to many more.

Prior to coming to Providence, where did you work?
I worked at OHSU, in Pediatric Neurology. Before that I worked at Cedars-Sinai Medical Center in Los Angeles, first on the inpatient rehab floor and then in the outpatient Spine Center.

So, what is your role as one of the nurses?
RNs in the specialty clinic arena wear many hats! Roles in which I am involved include:

- A LOT of telephone triage for all of our neurology providers. This may involve assessing a patient's current status to determine if he/she needs to be treated urgently in the ED, be seen in urgent care, by his/her PCP, or in person by his/her neurology provider.
- Providing education to patient and caregivers – on disease process and expectations, treatment process and expectations, medications, side effects, medication administration/injections and on when to call us or seek emergency care or PCP care.
- Identifying barriers to education, communication and/or access, and following up to make sure patients understand their treatment plan AND how to implement it.
- Being a patient advocate and providing comfort and support to patients and their caregivers. While this is needed in many areas of nursing, I think neurology is a field in which this is particularly needed. As a nurse, I can serve as a liaison between patients and providers to offer support that they might not request from providers directly, offering them the opportunity to open up and get additional information to help ease their way.

Why did you decide to become a nurse?
Nursing is a second career for me. I was a Montessori school teacher for 9 years, teaching 3-6 year olds. While I loved that career, I had decided it was time for a new challenge. At that same time, my dad became ill with lung cancer that metastasized to his spine. I spent a significant amount of time with him helping and supporting through the various stages of his treatment – a 10 day ICU stay, time on both medical and surgical floors, inpatient rehab, outpatient chemo infusions, radiology, MRIs, PET scans, helping to figure out home needs, DME needs, and home health services.. and finally staying with him for 2 weeks in hospice. I saw first-hand the value of an RN, and the difference a good RN can make to both a patient and his/her caregivers. So… I went back to school to become a nurse.

What advice do you have for patients?
Take it a day at a time and stay positive. Reach out to trusted loved ones who you know will be able to offer you support and understanding. While feeling scared and stressed is normal, try to listen to your provider, and come prepared at follow up appointments with your questions and most important (to you) concerns to discuss. Also, bring along that someone you can trust to help support you, be an advocate for you, ask the questions you forget to ask, perhaps even be a scribe for you during the appointment, and help you to later remember all that was discussed.

What advice do you have for caretakers?
Recognize that the patient might be experiencing a lot of emotional turmoil, and do your best to provide support. Listen when they need to talk, provide advice when they ask, be their advocate.

What do you like to do outside work?
I like to go dancing! Latin dances, swing dances, Kizomba, Cajun, zydeco… I love to go to music and dance festivals – if I’m on vacation, that’s probably where I’m at. I also like to take yoga and ballet classes. I sit all day at work, so getting out and moving is not only great for the body but also for the mind and soul!

Who would you invite to your dream dinner party (alive or dead)?
Good question…likely some old French philosophers…and my grandmother because I think she’d enjoy it and would make hilarious comments to them!
Fatigue is defined as “a subjective lack of physical or mental energy that is perceived by the individual or caregiver to interfere with activities of daily living”. People with MS may experience fatigue in different ways including exhaustion, lack of energy, increased sleepiness, or worsening of MS symptoms with fatigable weakness, made worse by activity and heat.

Several mechanisms from the disease process in MS might contribute to fatigue. Inflammatory cytokines, the cell signaling molecules that aid cell-to-cell communication in immune responses, are implicated in the MS disease process and are thought to be strong mediators of fatigue. The endocrine system is another possible contributor, through dysfunction of the hypothalamo-pituitary-adrenal axis. Fatigue could also be related to brain lesions, cortical atrophy, axonal damage, and hyper-activation of neural circuits. Overall, fatigue most likely represents a physiological adaptation to a weakened internal condition which is unable to meet external demands, where the brain of a person living with MS needs to work much harder to pass along messages.

Secondary causes for fatigue in MS exist as well. Sleep disorders are a common cause of daytime fatigue, and conditions such as Restless Legs Syndrome and Periodic Limb Movement Disorder may be more common in MS. Sleep apnea is common in the general population and can also affect MS patients. Chronic insomnia can arise in MS patients secondary to pain, spasticity, depression, anxiety, nighttime urination, and medication effects. Fatigue is strongly correlated with depression, which is also very common in MS. People with MS who are experiencing depression have greater fatigue and symptoms such as lack of motivation and inability to complete tasks. Fatigue is unlikely to improve if depression is present, so treatment with an anti-depressant is recommended. Some MS treatments, including anti-spasticity medications, pain medications, and interferon beta also have fatigue as a common side effect.

If other causes for fatigue are ruled out, people with MS can try both medications and non-pharmocologic measures to address fatigue. Non-pharmocologic measures include cognitive behavioral therapy, relaxation therapy, aerobic exercise via a graded exercise program, energy conservation strategies, use of cooling devices, avoidance of hot humid conditions and a low fat, low cholesterol diet supplemented with olive oil capsules.

Heat is often a cause for worsened fatigue during the summer months, as elevated temperatures further impair the ability of a demyelinated nerve to conduct electrical impulses properly. Some tips in beating the heat include:

- Drink plenty of fluids - preferably cool water - throughout the day. Icy drinks or popsicles can provide temporary relief.
- Stay in an air-conditioned environment during periods of extreme heat and humidity. The cost of an air conditioner may be tax deductible if a physician has written a prescription for it.
- Wear cooling garments such as vests, headbands and neckbands during exercise or outdoor activity; be aware of the added weight of a cooling vest. A simple damp cloth or towel can be helpful if you don’t have a cooling product.
- Exercise in a cool environment, such as an indoor mall or an air-conditioned gym. Pick cooler times of the day to exercise outside, such as early morning. Exercising in cool water (80-84 degrees) is an excellent way to combat heat during physical activity. Try pre-cooling before exercise; get into a bathtub of comfortably lukewarm water and add cooler water for 20-30 minutes.
- A cool bath or shower can help reduce core body temperature following activity or exposure to heat.
- Wear wide-brimmed hats and light-colored, loose clothing.
- Don’t overdo it, especially when you’re outside in the heat. Know your own limits.

References:


**Study Title: Pacific Northwest Multiple Sclerosis Registry**

**Objective:** The purpose is to measure MS prevalence in the Pacific Northwest and to create a database for ongoing epidemiological and health services research. Register at www.pacificnwms.org

**Sponsor:** Providence Health & Services  
**Principal Investigator:** Stanley Cohan, MD, PhD  
**Project Manager:** Tamela Stuchiner

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**Study Title: North America Registry for Care and Research in Multiple Sclerosis (NARCRMS)**

**Objective:** The primary objective is to develop a national longitudinal database in multiple sclerosis to capture, in a standardized manner, information from individuals with MS regarding their disease course from inception of the disorder through the lifespan of the individual.

**Sponsor:** Consortium of MS Centers  
**Site Principal Investigator:** Stanley Cohan, MD, PhD  
**Study Coordinator:** Lynette Currie

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**Study Title: Providence Ocrelizumab Patient Registry**

**Objective:** The goal is to collect information from patients receiving ocrelizumab for the treatment of MS to assess its long-term utilization, safety, tolerability and efficacy.

**Sponsor:** Providence Health & Services  
**Principal Investigator:** Kyle Smoot, MD  
**Study Coordinator:** Lois Grote

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**Study Title: Evaluating the Potential Role of Melatonin in Patients with Relapsing Multiple Sclerosis**

**Objective:** The study will evaluate the change in melatonin and melatonin metabolite level in blood and urine and assess the effect of melatonin on quality of life.

**Sponsor:** Providence Health & Services  
**Principal Investigator:** Kyle Smoot, MD  
**Study Coordinator:** Hannah Voss
Clinical Studies | Enrollment, continued

**Study Title: Multi-Center, Randomized, Double-Blinded Assessment of Tecfidera in Extending the Time to a First Attack in Radiologically Isolated Syndrome (RIS) (ARISE)**

**Objective:** To prospectively study the efficacy of Tecfidera in extending the time to a seminal acute or progressive demyelinating event in a cohort of U.S. RIS subjects.

**Sponsor:** UT Southwestern  
**Principal Investigator:** Stanley Cohan, MD, PhD  
**Study Coordinator:** Anne Gendreau

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**Study Title: A Traditional Versus Early Aggressive Therapy for Multiple Sclerosis (TREAT-MS)**

**Objective:** To evaluate, independently among patients deemed at higher risk vs. lower risk for disability accumulation, whether an “early aggressive” therapy approach, versus starting with a first-line therapy, influences the intermediate-term risk of disability accumulation.

**Sponsor:** John Hopkins University School of Medicine  
**Principal Investigator:** Kiren Kresa-Reahl, MD  
**Study Coordinator:** Hillary Frey

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**Study Title: A 3-Arm, Multicenter, Double-Blind, Placebo-Controlled, Randomized Study to Assess the Efficacy and Safety of ADS-5102 Amantadine Extended Release Capsules in Multiple Sclerosis Patients with Walking Impairment (ADAMAS)**

**Objective:** To evaluate the efficacy of 274 mg ADS-5102 in subjects with multiple sclerosis with walking impairment as measured by the Timed 25-foot Walk, the Timed Up and Go test, and the 2-minute Walk Test.

**Sponsor:** Adamas Pharmaceuticals, Inc.  
**Principal Investigator:** Kiren Kresa-Reahl  
**Study Coordinator:** Hannah Voss
Study Title: Measurement of Relaxin in the Serum and Cerebrospinal Fluid of Subjects With and Without the Relapsing Form of Multiple Sclerosis (RELAXIN)

Objective: This study will evaluate relaxin (RLX) levels in patients with multiple sclerosis.

Sponsor: Providence Health & Services
Principal Investigator: Stanley Cohan, MD, PhD
Study Coordinator: Hannah Voss

Study Title: Evaluating the Efficacy and Safety of Transitioning Patients From Natalizumab to Ocrelizumab (OCTAVE)

Objective: The primary objective of this study is to assess the efficacy of ocrelizumab (Ocrevus) in Relapsing Multiple Sclerosis patients who have been previously treated with natalizumab (Tysabri) by evaluating relapse rate, progression on MRI and disability progression.

Sponsor: Providence Health & Services
Principal Investigator: Kyle Smoot, MD
Study Coordinator: Genevieve Leineweber

Study Title: Long-term, Prospective, Multinational, Parallel-cohort Study Monitoring Safety in Patients With MS Newly Started With Fingolimod Once Daily or Treated With Another Approved Disease-modifying Therapy (PASSAGE)

Objective: The purpose of this world-wide prospective parallel-cohort study in patients with relapsing forms of Multiple Sclerosis, either newly treated with fingolimod or receiving another disease-modifying therapy, is to further explore the incidence of selected safety-related outcomes and to further monitor the overall safety profile of fingolimod under conditions of routine medical practice.

Sponsor: Novartis Pharmaceuticals
Site Principal Investigator: Stanley Cohan, MD, PhD
Study Coordinator: Lynette Currie
Study Title: Measuring the Impact of Tecfidera on the Gut Microbiota: Does a Change in the Gut Flora Correlate With Gastrointestinal Disturbances Following Therapy Initiation?

Objective: The primary objectives of this study are to determine whether a measurable change in bacterial species representation follows the institution of DMF (Tecfidera); to determine whether a specific pattern of change in the microbiota phylotype with DMF therapy correlates to onset and severity of gastrointestinal disturbances (heartburn, nausea, flatulence, and diarrhea); to determine whether any instability of microbiota phylotype representation persists following the institution of DMF or whether stabilization relates to resolution of gastrointestinal disturbances; and to determine whether there is a correlation between a pre-existing functional bowel disorder and development or severity of gastrointestinal disturbances and of peripheral eosinophilia.

Sponsor: Evergreen Health
Site Principal Investigator: Kyle Smoot, MD
Study Coordinator: Lynette Currie

For more information on clinical trials and research, visit us at oregon.providence.org/our-services/c/clinical-trials-brain or clinicaltrials.gov
Clinic News

JOIN US FOR MS YOGA

Are you living with Multiple Sclerosis and seeking ways to manage symptoms and improve wellness? Join Providence Brain and Spine Institute's monthly yoga class especially for people with MS.

Research has shown that several principles of yoga including body awareness, breath work, mobility and mindfulness can improve MS symptoms. This monthly class, taught by certified instructors, will lead people living with multiple sclerosis through 60 minutes of gentle yoga practice followed by 15 minutes of community connection and healthy habit sharing. Classes are FREE, but space is limited, so pre-registration is required.

**WHEN:** every 3rd Thursday of the month from 6:30 p.m. to 7:45 p.m. starting March 21st

**WHERE:** Basecamp, Providence St. Vincent Medical Center 9427 SW Barnes Rd, Mother Joseph Plaza, First Floor

**REGISTER:** 503-574-6595 OR PROVIDENCE.ORG/CLASSES

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…continued from page 1

guidance molecule isoform a (RGMa), which inhibits axonal growth. Therefore, symptoms and deficits related to MS possibly could improve.

In addition, several small studies evaluating the role of stem cells in repairing the damage caused by MS are underway. These cells are harvested from the body (mesenchymal stem cells (MCSS), neural stem cells (NCSs), or induce pluripotent stem cells (iP-SCs)), reproduced, and then re-introduced into the body either through the spinal fluid or blood. This procedure does not require the destruction of other immune cells, so there should not be a risk of infection. The hope is that these stem cells will go to areas of damage and facilitate repair of the nervous system.

These are only a few examples of possible treatment options that may help repair the nervous system resulting in clinical improvement. It is likely that more therapies will emerge as we gain a better understanding of the disease process.
Join Us at MS Society Events!

SAVE THE DATES

**Walk MS:**
Portland 2019
DATE: Saturday, May 11
LOCATION: Oregon Zoo
TIME: 8:00 a.m.

**Pathways to a Cure:**
Portland 2019
DATE: Saturday, July 13
LOCATION: Providence St. Vincent Hospital
TIME: 10:00 a.m.

**Bike MS:**
Monmouth, OR
DATE: Friday, August 2 through Sunday, August 4
LOCATION: Western Oregon University

**JUMPSTART MS:**
Portland 2019
DATE: Saturday, August 10
LOCATION: Providence St. Vincent Hospital
TIME: 9:00 a.m.

**PROVIDENCE BRAIN AND SPINE INSTITUTE IS A PROUD SPONSOR OF THE OREGON & SOUTHWEST WASHINGTON CHAPTER OF THE NATIONAL MS SOCIETY**

More information available at nationalMSsociety.org
JOIN THE MULTIPLE SCLEROSIS REGISTRY

WHAT IS THE PACIFIC NW MS REGISTRY?
The Pacific NW MS Registry was developed to measure MS prevalence in the Pacific Northwest and to create a database for ongoing epidemiological and health services research. The goal of the registry is to provide an accurate assessment of the number of individuals living with MS in the Northwest and to learn more about the course of the disease.

WHAT HAPPENS ONCE I SIGN UP?
We will send you surveys one or two times per year to learn about you, your disease, and the treatments or services you use to help manage your disease.
A number will be assigned to represent your information; therefore your name will never be linked to your clinical information. All information you provide will be secured.

HOW IS INFORMATION ABOUT ME USED?
The information you and other persons with MS provide will be used only for research purposes. Your personal identity will not be shown as part of any reports or made available to insurance or other companies. Only MS Registry researchers will have access to the information you provide, and your name and contact information will only be used to send you follow-up surveys or information about the registry.
Data will be used to describe the population living with MS in the Pacific Northwest. This information has the potential to be used to inform health policy as well as clinical and scientific advances. Individual data will not be used in scientific publications or presentations.

PARTICIPATION IS VOLUNTARY
You are not required to answer all survey questions, and you will not receive payment for participating. Also, you may choose to stop your participation at any time. If you decide to stop taking part in the MS Registry, please notify us by using the Pacific Northwest MS Registry contact information. Information that you have already provided will still be included as part of the registry, but no more information about you will be collected.

HOW DO I PARTICIPATE?
To sign up or learn more about the registry:
www.pacificnwms.org
Phone: 503-216-1022
Email: msregistry@providence.org
Providence Multiple Sclerosis Center

Our Providence Multiple Sclerosis Center team specializes in:
- Comprehensive MS care
- Neurology
- Neuro-ophthalmology
- Neurotology (for ear disorders)
- Nursing
- Physical therapy
- MS research

Clinicians:
- Stanley Cohan, M.D., Ph.D., Neurologist; medical director of Providence Multiple Sclerosis Center
- Kiren Kresa-Reahl, M.D., Neurologist
- Elisabeth Lucassen, M.D., Neurologist
- Meghan Romba, M.D., Neurologist
- Kyle Smoot, M.D., Neurologist
- Leah Gaedeke, FNP, Multiple Sclerosis Nurse Practitioner

Nurses:
- Sam Brighton, RN, BSN, Clinical Case Manager
- Amy Monroe, RN, BSN, Clinical Support Specialist
- Kiana Oskooii, RN, BSN, Clinical Support Specialist

Providence Multiple Sclerosis Center, the only center of its kind in Oregon, is the state’s leading care provider for people with MS. Our medical director, Stanley Cohan, M.D., Ph.D., was an investigator in the original, pivotal trial of beta interferon 1-A, one of the key medications for treating multiple sclerosis. He continues to play a leading role in MS research and founded the Pacific Northwest Multiple Sclerosis Registry Project, which will be used to help advance treatment of multiple sclerosis.

Our goal at Providence Multiple Sclerosis Center is to provide persistent, proactive, focused treatment that minimizes the effects of MS on your life. Patients benefit from comprehensive services that may include medication therapy, physical rehabilitation, counseling and other support. In addition, patients have access to the newest therapies through regional and international clinical trials.

Services:
- Highly advanced diagnostics
- Personalized treatment plans
- Attentive use of medications
- Rehabilitation with therapists who specialize in MS care
- Continence treatment for bladder and bowel dysfunction
- Emotional support and psychological counseling
- Opportunities to receive investigational medicines through clinical trials
- Close coordination with your primary care physician
- The Pacific Northwest Multiple Sclerosis Registry Project, a database created for epidemiological and health services research
- An MS Network that allows physicians to collaborate on MS treatments
- Community and provider education forums throughout Oregon

The Providence Multiple Sclerosis Center’s research is supported by generous donations from friends in the community. If you are interested in learning more about supporting the center’s work, please contact Dawn Johnston, Director of Development, at (503) 216-2198.
Available on our Web site at providence.org/brain:

- **Physician directory:** Get contact information for all Providence Brain and Spine Institute physicians.
- **Upcoming events:** Providence offers educational events throughout the year. Check our online calendar to view upcoming topics.
- **Clinical trials:** Find out about multiple clinical trials for investigational treatments for MS, as well as other clinical trials available through Providence.
- **Support groups:** Get details on support groups in Oregon.
- **Additional resources:** Our website offers the latest information on available programs and services; educational toolkits; and links to trusted sources of information.

**News & Events:**

- The MS Support Group meets for lunch from noon-1:00 p.m. on the first Thursday every month. Springwood Conference Room: Providence St. Vincent Medical Center, Mother Joseph Plaza. Lunch is provided.
- MS Yoga is now monthly! Join us from 6:30-7:45 p.m. on the third Thursday every month. The Well @ Basecamp: Providence St. Vincent Medical Center, Mother Joseph Plaza. Pre-registration required – please see page 8.
- Dr. Lucassen & Dr. Romba are now seeing patients twice a month at Providence Willamette Falls Medical Center.

**Providence Multiple Sclerosis Center**

9135 SW Barnes Road, Suite 461
Portland, OR 97225

(503) 742-6900

**Providence Neurological Specialties – Willamette Falls**

1510 Division St, Suite 180
Oregon City, OR 97045

(503) 742-6900

**Our Mission**

As expressions of God’s healing love, witnessed through the ministry of Jesus, we are steadfast in serving all, especially those who are poor and vulnerable.

**Our Core Values**

Compassion, Dignity, Justice, Excellence, Integrity

For the latest information, visit our blog at BrainAcademy.Providence.org