Fall 2019

MS Perspectives™

Volume 12, Issue 1

Practical Insights on Multiple Sclerosis

In This Issue

- MS Categories Defined—and Redefined
- Real-life Healthy Living Tips from People with MS

New Drugs for Secondary-Progressive and Relapsing MS

Page 4

This publication is supported by educational grants from Biogen, Celgene Corporation, and Novartis Pharmaceuticals Corporation.

Published in partnership with:

IOMSN
The International Organization of Multiple Sclerosis Nurses

www.MSperspectives.com

Publishing Information

Publishers
Joseph J. D'Onofrio
Frank M. Marino
Delaware Media Group
PO Box 937
Glen Rock, NJ 07452
jdonofrio@delmedgroup.com

Writer/Editor
Nancy Monson

Art Director
James Ticchio

Proofreader
Pete Kelly

MS CATEGORIES DEFINED– AND REDEFINED

To treat a disease, you have to understand it in all its varieties—and multiple sclerosis (MS) comes in several varieties. That's why it is important for clinicians to be able to separate MS into specific groups (or phenotypes). The phenotypes are based on characteristics of the disease like the age of onset, the pattern of progression or worsening, the presence or absence of relapses, and the pace of the disease. As treatment options have increased, MS clinicians have looked for ways to more accurately define the phenotypes and connect each disease pattern with the best treatment options for each individual patient.

This article will talk about how experts have traditionally classified different MS disease courses and how they're now classifying them in light of advances in the field.

Aliza Ben-Zacharia, DrNP
Nurse Practitioner, Neurology Assistant Professor
Associate Director of the Center for Nursing Research and Innovation
The Corrine Goldsmith Dickinson Center for Multiple Sclerosis
The Mount Sinai Hospital
New York, NY

The Traditional Classification

In 1996, the international MS community released an article describing four phenotypes for MS. This classification system separated MS into relapsing and progressive disease categories based on how the disease was described to clinicians by patients and their families (known as the clinical presentation) and how the disease changed over time as observed by the neurology team.

The four original subcategories were:

- **Relapsing-Remitting MS (RRMS)**. People with RRMS were categorized as having flare-ups of symptoms, also called attacks or exacerbations, followed by remissions and periods of recovery during which they regained all or part of their function that had been affected by the MS flare-up. This is and was the most common type of MS, affecting 85% of people diagnosed.
- **Secondary-Progressive MS (SPMS)**. In the SPMS category, symptoms were known to worsen over time, with or without the occurrence of relapses. In addition, SPMS was defined as a phase of the disease that could only occur after a period of having RRMS.
- **Primary-Progressive MS (PPMS)**. PPMS was characterized by slowly worsening symptoms from the onset of the disease, with no relapses.

Cover photo credit: ©Kesu01 / iStock

- **Progressive-Relapsing MS (PRMS)**. Affecting just 5% of patients with MS, PRMS was characterized by a worsening disease state from the onset of the illness, with relapses with or without recovery of function.

These classifications were rapidly adopted into clinical practice and used in designing research trials.

Reclassifying MS

Moving forward, in 2013, MS experts released an updated classification system for MS subtypes based on new information learned from research and clinical experience.

The new classification system separates MS in two ways: Every patient is assigned a designation of having "active" or "not active" disease. Active disease means the person has had relapses or has a magnetic resonance imaging (MRI) scan that shows new lesions are developing or existing lesions are changing. Every patient is also assigned a designation of "progressive" or "not progressive" disease. Progressive disease means that the individual is experiencing a worsening of disability over time without evidence of any relapses.

MS clinicians continue to use the traditional phenotypes, but the updated classification system somewhat redefines them using additional information learned from MRI scans. The four types now are:

- **Clinically Isolated Syndrome (CIS)**: CIS is a first inflammatory episode of the central nervous system that may involve the eye (called optic neuritis), the spinal cord (called transverse myelitis), or the brainstem (called a brainstem episode). This may be an isolated event or it may be the first clinical presentation of what will go on to become MS. An MRI brain scan performed at the time of this first event may be normal or it may show "spots" that suggest there is inflammation going on in the central nervous system. Up to 85% of people who have a CIS event go on to develop MS within the next 2 years, which is why it is included in the updated classification system (and often treated).
- **RRMS.** Still the most common disease course and described as above, RRMS is now broken down into active or not active subcategories, and progressive (worsening) or not progressive subcategories. MS is considered to be active if you've had clinical relapses within the past year or there is evidence on your MRI scan of new lesions or changing lesions. Likewise, RRMS is considered to be progressive if your disability is worsening even when you're not having a relapse. So you can have active RRMS with progression, active RRMS without progression, not active RRMS with progression, or stable disease, meaning not active RRMS without progression. Since the 1990s, over a dozen disease-modifying therapies (DMTs) have been approved by the Food and Drug Administration (FDA) that may delay the progression of RRMS and lessen relapses.
- **SPMS**. This type of MS usually develops after people have had an RRMS disease course for many years and are experiencing more and more disability. It can be difficult for clinicians to know when people have transitioned from an RRMS disease course to an SPMS disease course because they can still have occasional relapses. Like RRMS, SPMS can be further categorized as active, not active, progressive, and not progressive. The emergence of DMTs has reduced the number of people who will develop progressive MS. And this year, for the first time, two drugs (cladribine, brand name Mavenclad®, and siponimod, brand name Mayzent®) were released onto the US market specifically for the management of active SPMS (see the next article in this issue, on page 4).
- **PPMS.** The definition of this phenotype is unchanged from 1996 (see page 2), but it is further categorized as active or not active and progressive or not progressive. Many MS experts believe that PPMS is a very different type of MS than RRMS. For many years, there was no treatment for this type of the disease, but in 2017 a drug called ocrelizumab (Ocrevus®) was approved by the FDA to treat PPMS and relapsing forms of MS. PPMS affects about 15% of patients with MS.

You may notice that a syndrome known as radiologically isolated syndrome, or RIS, is not considered to be part of the spectrum of MS phenotypes. That's because patients with RIS lack clinical signs and symptoms of MS; instead their MRIs show what could or could not end up being MS lesions. These lesions are found when a person has an MRI scan for a problem unrelated to MS—say migraine headaches. Experts believe that 25% of patients with an RIS finding may convert to MS, but until more information is available, RIS is not typically treated.

NEW DRUGS FOR Secondary-Progressive and Relapsing MS

As the number of multiple sclerosis (MS) medications has expanded for people with relapsing-remitting disease, there hasn't been much action on the progressive disease front. In part, that's because progressive disease behaves very differently than relapsing disease, and it's been difficult for researchers to get a handle on what the real problems are and how to solve them. Last year, a big step forward was achieved for people with primary-progressive MS (PPMS) when ocrelizumab (Ocrevus®) was approved by the Food and Drug Administration (FDA). It's still too early to tell if and how well the drug is working to prevent progression in PPMS, but we are hopeful. And this year, we have two new drug approvals for people with active secondary-progressive MS (SPMS): cladribine (Mavenclad®) and siponimod (Mayzent®). (See the cover story on page 2 for a description of how relapsing and progressive forms of MS are now categorized as active or not active, and worsening or not worsening.) These new drugs are also approved to treat relapsing MS, and Mayzent® is also approved for clinically isolated syndrome.

Mavenclad®

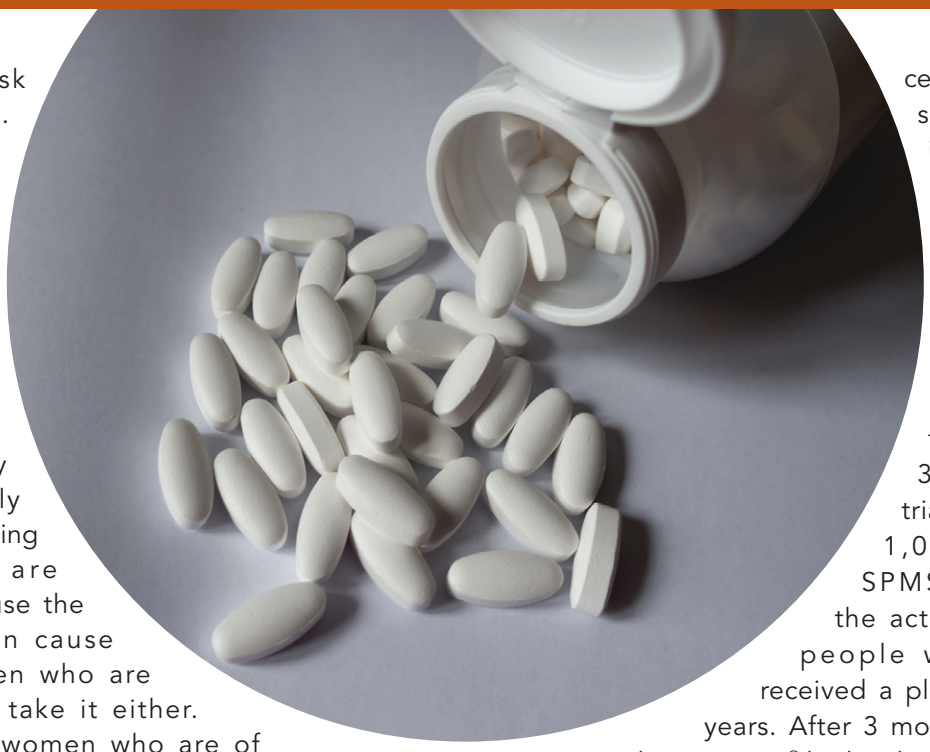
This oral drug is a totally unique disease-modifying therapy (DMT) that was approved by the FDA in March 2019 to treat active SPMS and relapsing forms of MS; it is also available in 50 other countries around the world. Mavenclad® is believed to decrease the numbers of white blood cells called lymphocytes in the immune system that cause the nerve damage associated with MS.

Barbara J. Green, MD
MS Center for Innovations in Care
Missouri Baptist Hospital
St. Louis, MO

The drug is taken by mouth over the course of 2 months for 2 years in a row. The medication dose is calculated based on a person's weight. The first half of the total dose is taken for 4 to 5 days over 2 months during the first year of use. The second half of the dose is taken in exactly the same way in year 2. It's not yet known how long the drug's effects will last or if other DMTs will need to be given, but it is known that this drug can't be taken again for 4 years after the 2-year dosing regimen.

Several randomized, double-blind, controlled studies have been performed showing Mavenclad® is effective in reducing relapse rates, magnetic resonance imaging (MRI) activity, and the progression of disability. In the CLARITY trial involving 1,326 patients, which was the basis for its FDA approval, Mavenclad® was found to reduce the annual relapse rate by 58%. The drug worked as well in people with highly active disease and without more side effects as it did in those with less disease activity. For 2 years following the end of treatment, 81% of people who had received Mavenclad® did not have any relapses compared with 63% of people who received a placebo.

Infections, such as colds, urinary tract infections, and shingles, are a common side effect of Mavenclad®, as is headache. Because Mavenclad® is a high-potency drug that lessens lymphocytes, it can lower lymphocyte counts too much, which



can increase the risk for these infections. No cases of the serious infection progressive multifocal leukoencephalopathy (PML) have been seen with the drug, however, as they have with some other DMTs. Mavenclad® can't be used by people who currently have infections, including HIV. Women who are pregnant also can't use the drug because it can cause birth defects; women who are breastfeeding can't take it either. And both men and women who are of reproductive age must use effective birth control while taking Mavenclad®, as they need to with most DMTs.

Data from several clinical trials that looked at the long-term safety of Mavenclad® show a slight increase in cancer cases among people taking the drug compared to people taking a placebo. As a result, routine cancer screenings and prevention are recommended for all people taking this DMT.

The FDA is recommending it for people who have not responded well to at least one other DMT. For these people, Mavenclad® is an attractive option because of the short courses of treatment and the potential for long-term benefit.

You will need to have blood tests before you can start the drug, and receive vaccinations if you're not immune to common infections. You will also need to come into your MS clinician's office for follow-up laboratory tests, to ensure that your lymphocyte and complete blood counts haven't gotten too low and that the drug isn't affecting the liver.

Mayzent®

Mayzent® is another oral drug that stops lymphocytes from entering the central nervous system and causing damage. It is in a class of drugs known as sphingosine 1-phosphate (S1P) receptor modulators (S1P receptors being those that are found on the outside of immune cells). Mayzent® is the second medication in this class to be approved by the FDA; fingolimod (Gilenya®) was the first.

The approval of Mayzent® was based on the results of the 31-country EXPAND trial, which included 1,099 people with SPMS who received the active drug and 546 people with SPMS who received a placebo for up to 3 years. After 3 months, it was found that Mayzent® had reduced the progression of disability by 21% compared to placebo. It was even more effective for people with more active disease, reducing disability progression by 33% versus placebo in people who had had relapses over the 2 years before entering the trial.

Mayzent® can cause many of the same side effects as Gilenya®, such as liver function abnormalities and eye problems. Also like Gilenya®, Mayzent® has the potential to cause PML. Unlike Gilenya®, which may significantly slow the heart rate on the first day of use requiring that patients be observed for 6 hours after taking the drug, Mayzent® causes fewer initial cardiac effects and stays in the body for a shorter period of time. So while the heart rate may slow, it's not usually as much cause for concern. An increased risk of infections is also common with this drug, since it lowers the number of lymphocytes in the blood. The most common side effects of Mayzent® are headache, high blood pressure, and liver abnormalities. As with Mavenclad® and many other DMTs, you need to visit your clinician for follow-up laboratory tests while on Mayzent®.

The FDA approved Mayzent® to treat active SPMS, relapsing forms of MS, and clinically isolated syndrome. However, it should not be used by women who are pregnant, breastfeeding, or want to conceive, or those with significant abnormal heart rhythms (arrhythmias) or other heart problems.

REAL-LIFE Healthy Living Tips
from People with MS

Who better to give advice about living healthy while having multiple sclerosis (MS) than other people who have the disease? MS Perspectives™ asked some readers for their best tips.

Diagnosed with relapsing-remitting MS in 2000, **Rose Ann Behson**, a schoolteacher, responded by taking up running. "I decided when I got MS not to let it get to me. I go to the gym regularly, I play tennis, and I run." When she has a flare-up, she still runs, just slower and less frequently. "Even if you can't do a full workout, do something every day," she advises.

To avoid overheating, she doesn't wear socks while running, and wears minimal clothing. "When the temperature is 40° to 50° F, I'll be out in a sports bra and shorts to keep cool." She also finds that having a daily stretching routine helps with spasticity in her muscles.

Her husband has made a big effort to be a full support partner and makes sure they both eat well. "We buy organic produce and we grow our own vegetables," she says. "It's a little more expensive to buy organic, but we know we're not getting pesticides and artificial ingredients."

She also turns to Facebook groups for support. "There are all sorts of very specialized groups you can join on Facebook to ask questions and share information. I am open about having MS in my life, because I figure you never know who you can help or who can help you."

Rose Ann says, "Don't think the worst, and don't give up. There are things you can't control but attitude plays a big role in how your life plays out. I didn't know there would be new drugs when I was first diagnosed, and now I haven't had a relapse in a long time."

David Mogil has had MS for 33 years. "I had my first episode when I was in my last year at St. Louis University School of Law. I was 27," he says. Today, he has been told that his MS is somewhere on the spectrum between relapsing-remitting and secondary-progressive MS.

David is now retired due to his disability, but stays busy with exercise—he's currently in a training program with "The Exercise Coach," a personally optimized strength-training plan that takes 20 minutes twice a week.

Faith plays a major role in his lifestyle. He and his wife are of the Jewish faith and observe the Sabbath from sundown Friday to sundown Saturday. "Since we do not do any work during this time and we are not wired or connected," he explains, "it is an ideal time to socialize with our friends and family."

David says that he tries to maintain an upbeat attitude, "especially on days that I may be fatigued. I have observed that a negative attitude is a people repellent, while a sunny disposition is a bit more engaging."

She also makes efforts to eat well. "To my knowledge, there is no proof of a special diet for MS, but eating fresh produce, less-processed foods, whole grains, and limiting fat can help keep our bodies at the right weight and give us the energy we need," she says. "One change I made years ago was to improve my breakfast. I enjoy oatmeal, a hard-boiled egg, plain Greek yogurt with fruit, or granola."

Lastly, Michelle advises learning all you can about the disease and how to manage your symptoms and adhere to your DMT. Also, expect and acknowledge that you will go through various coping "stages" from denial to anger, depression, bargaining, and acceptance, she says.

For health maintenance, **Michelle Keating**, a retired nurse who was diagnosed with RRMS in 1981 at the age of 25, makes exercise a priority every day by taking walks, stretching, riding a recumbent trike, or doing chair yoga to move her body. "At one point in my MS journey, I was using a scooter full time for about 10 years," she recalls, "but with a deliberate and disciplined effort to increase my exercise regimen, along with effective disease-modifying therapy (DMT) and God's grace, I was able to regain my mobility! This does not happen for everyone, but the tremendous benefits of exercise for strength, endurance, and fatigue are proven for all with MS."

She observes that "some days our goals may have to change due to MS symptoms. We learn there are limitations and we just need to adapt. For instance, a little extra time in the morning for my bowel routine frees me from worry about a bowel accident later in the day. And I find stretching in the morning helps me get moving a little easier."

Michelle has also found that tapping into creative hobbies enhances her life. "Knitting, quilting, writing, beading, and sewing have been important activities for me to give me hope and provide relaxation," she says. A study she conducted found that engaging in creative activities has positive effects on self-esteem and self-efficacy (the belief that you are competent and able) for people with MS.

Denise Pisciotta, a working CPA who uses a wheelchair, was diagnosed with secondary-progressive MS in 1989, but hasn't had a relapse in 20 years. Her number one tip is to always try to have a positive attitude. She advises asking for help when you need it, too. "A lot of us are stubborn and don't want to ask, but people are willing to help," she says. She relies on exercise to maintain her health, seeing a personal trainer twice a week and exercising at home using a standing frame. She also feels that it is important to maintain social connections: "Surround yourself with family and friends who are positive influences for you, keep you moving, and won't get upset or down that you have MS," she says.

Life Hack

Use technology to make life easier. This can range from using a smartphone app to an adjustable bed and devices that can turn on your lights and open your front door remotely.

Support Programs for MS Disease-Modifying Therapies (DMTs)

Aubagio,® Genzyme Corporation:
www.aubagio.com, 855-MSONE2ONE (855-676-6326)

Avonex,® Biogen:
www.avonex.com/en_us/home/above-ms-program/join-biogen-support.html, 800-456-2255

Betaseron,® Bayer HealthCare:
https://www.betaseron.com/why-betaseron, 844-788-1470

Copaxone,® Teva Neuroscience:
http://copaxone.com/AboutSharedSolutions.aspx, 800-887-8100

Extavia,® Novartis:
www.extavia.com/info/PatientSupport/patient-support-program.jsp, 866-EXTAVIA (866-398-2842)

Gilenya,® Novartis:
www.gilenya.com, 800-GILENYA (800-445-3692)

Glatiramer Acetate Injection, Mylan:
www.glatirameracetate.com/en/patient-support, 844-695-2667

Glatopa,® Sandoz:
www.glatopa.com, 855-452-8672

Lemtrada,® Genzyme:
www.lemtrada.com, 855-MSONE2ONE (855-676-6326)

Mavenclad,® EMD Serono:
www.mslifelines.com, 877-447-3243

Mayzent,® Novartis:
www.mayzent.com, 1-877-MAYZENT (1-877-629-9368)

Ocrevus,® Genentech:
www.ocrevus.com, 844-OCREVUS (844-627-3887)

Plegridy,® Biogen:
www.plegridy.com, 800-456-2255

Rebif,® EMD Serono:
www.mslifelines.com, 877-447-3243

Tecfidera,® Biogen:
www.tecfidera.com, 800-456-2255

Tysabri,® Biogen:
www.tysabri.com/en_us/home/join-biogen-support/join-biogen-support.html, 800-456-2255

MS News, Support, and Self-Help Groups

Can Do Multiple Sclerosis
www.mscando.org

MS Views & News
http://www.msviews.org/msviewsandnews4

MS World
www.msworld.org

Multiple Sclerosis Association of America
http://mymsaa.org, 800-532-7667

Multiple Sclerosis International Federation
www.msif.org

Multiple Sclerosis Foundation
www.msfocus.org, 888-MSFOCUS (888-673-6287)

National Multiple Sclerosis Society
www.nationalmssociety.org, 800-344-4867

Sign up for a free subscription to *MS Perspectives™*

Complete and cut out the card below and mail it to:
Delaware Media Group, PO Box 937, Glen Rock, NJ 07452-0937

Yes! I'd like to receive *MS Perspectives*™ ☐ by mail ☐ by email

Name _____

Address _____

City _____ State _____ ZIP _____

Email _____

The publisher values your privacy and the confidentiality of your personal information. We will use your contact information only to provide you with a free subscription to *MS Perspectives*™. Please be assured that your name will not be sold or distributed for any commercial purposes or otherwise.

Delaware Media GROUP

www.delmedgroup.com