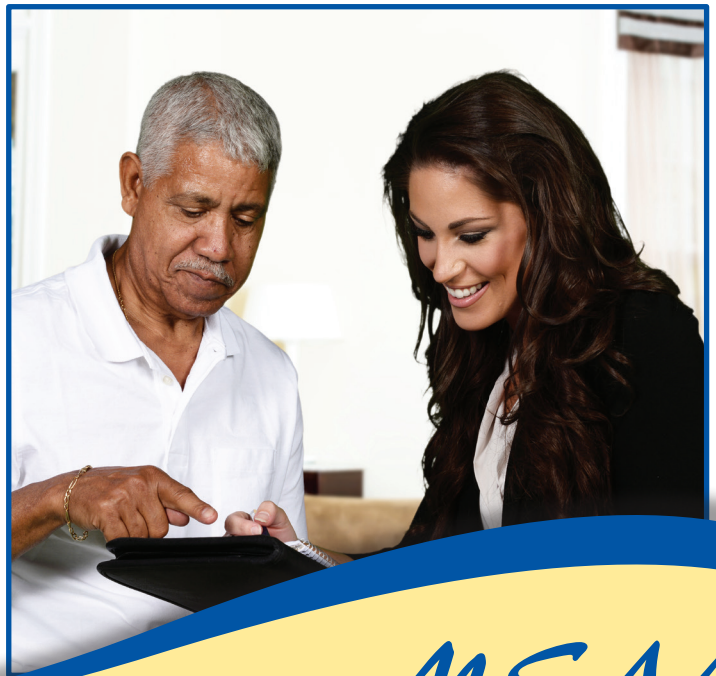


Understanding Progression in MS



MSAA

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Preface



The purpose of this booklet is to provide information on progression in multiple sclerosis (MS), largely focusing on the progressive forms of the disease: secondary-progressive MS (SPMS) and primary-progressive MS (PPMS), which are more challenging in terms of both information and treatment. Since a significantly greater percentage of the MS population starts out with relapsing MS, information on progression in MS can be more difficult to find. Additionally, in contrast to relapsing forms of MS, where

many treatments have been available for several years to slow disease activity, individuals experiencing progression in MS have had few, if any, treatment options.

However, times are changing for the better. In 2017, the first medication was approved by the United States Food and Drug Administration (FDA) to treat PPMS, along with relapsing forms of MS, which includes SPMS with relapses. Adding to this good news is the fact that several other experimental therapies are currently under investigation to determine their effectiveness on slowing disease activity and progression in MS.

This booklet starts out with general background information on MS, aimed to assist anyone who is not familiar with the disease. In the sections to follow, readers may learn about how progression is measured and assessed in MS, revised classifications of MS, what processes are involved in the development and worsening of the disease, treatment options, symptom management, how to discuss progression with one's neurologist, and wellness strategies.

For additional information on MS or to speak with one of MSAA's trained Client Services specialists, readers may call MSAA's Helpline at **(800) 532-7667, extension 154**. Questions to MSAA's Client Services department may also be emailed to **MSquestions@mymsaa.org**.

Part I:

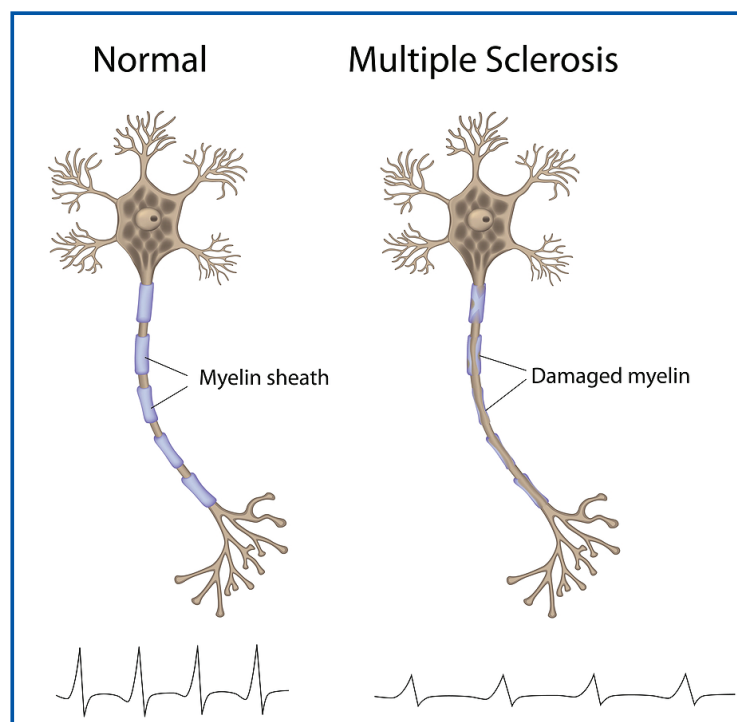
Understanding Progression in MS

Background Information

Multiple sclerosis (MS) is a disease of the central nervous system (CNS). The CNS consists of the brain, optic nerves, and spinal cord. With MS, areas of the CNS become inflamed, damaging the protective covering (myelin) that surrounds and insulates the nerves (axons). In addition to the myelin, over time, the axons and nerve cells (neurons) within the CNS may also become damaged. This damage is referred to as neurodegeneration.

The damage to the protective covering and also to the nerves disrupts the smooth flow of nerve impulses. As a result, messages from the brain and spinal cord going to other parts of the body may be delayed and have trouble reaching their destination – causing the symptoms of MS. Described later in this booklet, these symptoms can include a wide variety of physical, emotional, and cognitive changes.

Areas of inflammation and damage are known as lesions, which are viewed on magnetic resonance imaging (MRI) scans. The changes in size, number, and location of these lesions may determine the type and severity of symptoms. While individuals with relapsing forms of MS are believed to experience more inflammation than those with progressive forms of MS, lesions still occur for individuals with all forms of MS. However, the lesions in progressive forms of MS may be less active and expand more slowly.



Shown above is an illustration of two nerve cells. The normal one on the left has a healthy nerve fiber, or axon, protected by myelin (insulation covering the nerve), and is able to transmit signals at a very fast speed – similar to electricity traveling along an electrical cord. The MS nerve cell on the right shows damage to the myelin, and as a result, signals do not travel well along the nerve.

Types of MS

MS affects each person differently. For many years, the most common types of MS had been classified as:

- relapsing-remitting MS (RRMS)
- primary-progressive MS (PPMS)
- secondary-progressive MS (SPMS)
- progressive-relapsing MS (PRMS)

However, these classifications are changing, and some experts are now grouping relapsing-remitting MS (RRMS) and secondary-progressive MS (SPMS) together, as a continuum of the same disease. These are now frequently referred to as **“relapsing forms of MS.”** Additionally, progressive-relapsing MS (PRMS) and primary-progressive MS (PPMS) have also been grouped together. These are now frequently referred to as **“progressive forms of MS.”**

Initially, most people with MS experience symptom flare-ups, which are also known as relapses, exacerbations, or attacks. When someone experiences a relapse, he or she may be having new symptoms or an increase in existing symptoms. These usually persist for a short period of time, from a few days to a few months. Afterward, the symptoms greatly improve or remit completely, and these individuals may remain symptom-free for periods of months or years. This type of MS is known as relapsing-remitting MS (RRMS). Approximately 80 to 85 percent of MS patients are initially diagnosed with this form of the disease.

Over time, RRMS may advance to secondary-progressive MS (SPMS). This form of MS does not have the dramatic variations in symptoms that RRMS does, but rather has a slow, steady progression – with or without relapses. If relapses do occur, they usually do not fully remit.

Without treatment, approximately half of individuals with RRMS convert to SPMS within 10 years. However, with the introduction of long-term disease-modifying therapies (DMTs), fewer individuals advance to this latter form of the disease. Since 1993, and as of mid-2017, a total of 15 DMTs have been approved by the FDA and are available through prescription. All of these approved medications are aimed at slowing disease activity and delaying progression in MS.

Individuals who are not initially diagnosed with RRMS may be experiencing a more steady progression of the disease from the onset. Approximately 10 percent of the MS population is diagnosed with primary-progressive MS (PPMS), where individuals experience a steady worsening of symptoms from the start, and do not have periodic relapses and remissions.

Approximately 5 percent of patients are initially diagnosed with progressive-relapsing MS (PRMS). This type of MS steadily worsens from the onset, but symptom flare-ups – with or without remissions – are also present.

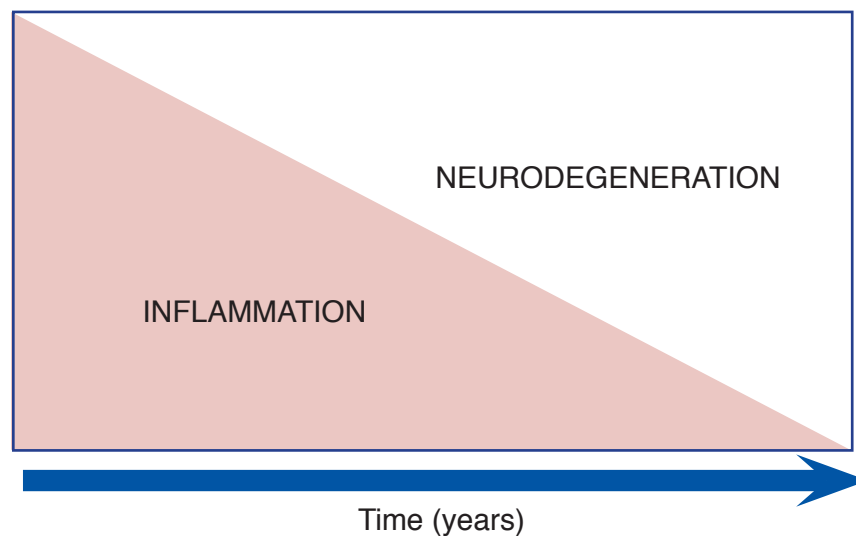
The Pathogenesis of MS Progression

All forms of MS share an underlying pathogenesis, which refers to the origin of a disease and its development. The pathogenesis of MS includes:

- **inflammation** – this is an autoimmune attack where an individual's own white blood cells cause damage to his or her own neurons within the brain and spinal cord
- **demyelination** – this is damage to the myelin covering around nerves, caused by inflammation
- **axonal degeneration** – this is the shrinking, atrophy, and death of neurons
- **remyelination** – this is the body's own attempt to repair damaged myelin, although this repair is often incomplete
- **glial scar formation** – this results in multiple scars within the brain and spinal cord at sites of damage from MS

Research has shown that individuals with progressive forms of MS have predominantly neurodegeneration and less inflammation. This is in comparison to relapsing-remitting MS, where inflammation is the predominant driver of the disease with less neurodegeneration occurring early in the disease process.

Multiple Sclerosis Pathophysiology



Particularly with relapsing forms of MS, inflammation is greatly involved with the initial disease process. This causes damage to the myelin – the protective covering of the nerves in the central nervous system – and eventually damage to the nerves as well. As time progresses and fewer relapses are experienced, the disease involves increasingly less inflammation and more neurodegeneration, which is the breakdown or cell death of nerve cells.



The Measures and Assessment of Progression

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) has revolutionized the ability to efficiently diagnose MS, track new inflammatory-disease activity – through the discovery of new T2 bright spots and/or new gadolinium-enhancing lesions (these are areas of disease activity with inflammation) – as well as monitor an individual's response to MS disease-modifying therapies. Currently, an MRI scan provides the best biomarker for evidence of MS progression. MRI measures that most closely correlate to progression include:

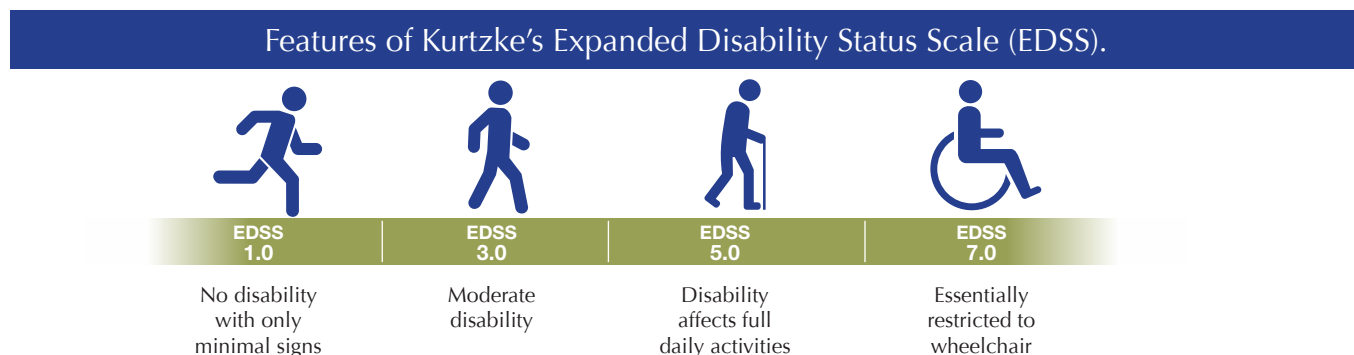
- accelerated brain atrophy, which refers to faster brain shrinkage
- development of T1 hypointensities, also referred to as “black holes,” which indicate more neurodegeneration versus inflammation

Readers should note that many of the current MS therapies have been shown to decrease the accumulation of bright spots and black holes as viewed on an MRI, along with slowing atrophy rates. MS specialists encourage people with MS to review their MRI scans with their providers and to ask about these two types of disease measures.

Important note: MSAA may be able to help cover MRI costs through its **MRI Access Fund** program (certain income limits apply). To learn more, please visit mymsaa.org/mri or call (800) 532-7667, extension 120.

The EDSS and Neurologic Exam

Kurtzke's Expanded Disability Status Scale (EDSS) is the oldest and most widely accepted measure of MS disability. The EDSS ranges from 0 to 10 in half-point increments, where 0 is a normal examination, 3.0 is moderate disability, 6.0 is where the person needs assistance to walk, and higher numbers refer to greater disability, largely in terms of mobility.



Shown above are features from Kurtzke's Expanded Disability Status Scale (EDSS). Frequently used for clinical evaluation and research study assessments, it mainly focuses on mobility when determining a score.

A trained MS clinician assigns a functional score to a patient in eight neurologic systems: pyramidal (referring to the motor system, with weakness and spasticity), cerebellar, brainstem, sensory, bladder and bowel, vision, cerebral, and "other." These are all based on a standard neurologic examination. The EDSS is frequently criticized for being insensitive to small changes, being heavily dependent on mobility, not capturing cognitive impairment, being subjective in some assessments (rating scores can vary), and for not capturing the full range of disabilities.

The Multiple Sclerosis Functional Composite

The Multiple Sclerosis Functional Composite (MSFC) is another clinical tool that assesses MS disability. Unlike the EDSS that is based on a standard neurological examination, the MSFC assesses disability using three "functional" tests. It summarizes the scores of the following:

- a timed 25-foot walk evaluating ambulation
- the nine-hole peg test evaluating arm function
- the paced auditory serial addition test evaluating cognition

The goal of this system is to capture information on key functional measures affected by MS, specifically leg, arm, and cognitive function. The MSFC is often used in connection with the EDSS in MS clinical trials. Many aspects of the MSFC, such as the timed 25-foot walk, are routinely monitored in MS clinics as well.

The Natural Progression of MS

Approximately one in every 750 individuals in the United States has MS. The natural progression of MS has changed over time. Early studies showed that the median time from onset of PPMS to needing a device (such as a cane) to assist with walking was 10 years, while more contemporary studies show that this has increased to 15 years. Another study showed that 25 percent of people with PPMS still did not require a cane after more than 25 years. Although difficult, individuals with MS should not compare their disease course with those of others, as every individual is different.

Risk factors for disease progression have been identified, but their interplay is complex. Early onset of disease and female gender are favorable factors associated with a better prognosis in terms of one's long-term course of MS. For instance, individuals who were young at the onset of their MS have been shown to take a longer amount of time before their MS progresses to the point of needing a device to assist with walking, which is a score of 6.0 on the EDSS.

Relapses can still occur in people with progressive MS. Individuals with secondary-progressive MS can have an occasional relapse, which is a new neurologic symptom that lasts more than 24 hours, in the absence of fever or infection. This occasional relapse is superimposed on progressive disease, characterized by a gradual decline.

For example, an individual with SPMS may notice worsening balance and walking issues over several years, and then notice over the course of hours to days, they have developed blurry vision in one eye and pain with eye movements. He or she may then be diagnosed with an MS relapse of optic neuritis, in addition to having a gradual decline in neurologic function over the course of years. This is different from RRMS, as individuals with RRMS only experience neurologic worsening in the setting of a relapse.

Criteria for Diagnosis and Description Modifiers

The word “progressive” has historically carried a negative connotation among members of the MS community. However, when this term was first coined, the understanding of the pathophysiology of MS – which is how the disease progresses and its effects – was very limited. Neuro-diagnostics, which use advanced technology to diagnose, evaluate, and sometimes treat certain neurological conditions, were in their infancy, and the therapies that could slow progression were lacking. Fortunately, the MS world is changing.

Currently, no criteria have been defined to determine definitively when a person with MS has progressed from RRMS to SPMS. However, criteria are in place for a diagnosis of SPMS, which requires the onset of the disease with at least one clinical relapse (differentiating it from PPMS), followed by a gradual decline in neurologic function over the course of at least six to 12 months. This decline must be separate from the worsening that occurs during relapses.

The diagnosis of PPMS has distinct criteria based on 2010 McDonald criteria for the diagnosis of MS. To receive a diagnosis of PPMS, a person with MS must have one year or more of gradual decline in neurologic function, in addition to two or more of the following:

- abnormal lesions consistent with MS on MRI
- two or more lesions consistent with MS in the spinal cord
- cerebrospinal fluid (CSF) analysis consistent with the diagnosis

Individuals with RRMS are usually diagnosed between the ages of 15 and 40. The average age of onset of SPMS and PPMS is in the fifth and sixth decades of life, when people are in their 40s or 50s. While RRMS often affects women two-to-three times more often than men, the gender ratio in PPMS is equal between males and females.

In both SPMS and PPMS, the rate of decline in neurologic function occurs at a similar rate. Individuals with PPMS generally have more spinal-cord lesions than those with SPMS. It is important to note that the diagnosis of the type of MS is based on clinical history, which is determined through doctor visits and evaluations. Progressive forms of MS cannot be diagnosed with an MRI or spinal-fluid analysis alone.

As part of the 2013 International MS Phenotype Group revised MS classification criteria, three important modifiers were added to the description of MS: activity, worsening, and progression. These modifiers help to more accurately reflect the current disease process in a specific individual with MS.

- **Disease activity** refers to a new clinical MS attack (relapse) or a new bright spot (showing inflammation) on the MRI.
- **Disease worsening** simply reflects that a specific person's neurological examination has gotten worse compared to prior examinations, possibly related to an MS attack (relapse).
- **Disease progression** indicates worsening on an exam, independent from an attack (relapse).

In summary, people with progressive MS can and do have attacks (relapses), albeit infrequently, and develop new spots (or lesions) on MRI. Both relapses and new lesions are types of disease activity. Additionally, MS may be “clinically silent,” showing no increase in symptoms, yet continuing to show signs of disease activity within the CNS, as seen on MRI. Conversely, these same people can experience long periods of time without progression and without worsening. These variations in disease activity show how dynamic MS is, while affecting each individual differently.

Non-MS Causes of Clinical Worsening

Clinical worsening in MS, or the gradual decline in function, should not immediately be attributed to MS as the only cause. Individuals with MS can also acquire other medical problems that can mimic MS progression. These include:

- cervical stenosis – a narrowing of the spinal canal in the neck, which can put pressure on the spinal cord and cause a worsening of gait, sensation, strength, as well as a worsening of bowel and bladder control
- vitamin deficiencies, such as B12
- thyroid disease
- other conditions not related to MS

As a result, a thorough evaluation by a neurologist as well as a regular follow up with a primary-care physician are important. If alternative causes are ruled out, then a neurologist may confirm that progression is directly related to one's MS.



Part II: Treating Progression in MS



Disease-Modifying Treatment Approaches Targeting Inflammation

The greatest success in MS has been in treating relapsing forms of MS. Relapsing forms of MS largely involve inflammation and nearly all of the approved disease-modifying therapies (DMTs) are approved to treat these types of MS. These DMTs have been shown to:

- Reduce the number and severity of relapses
 - Reduce the development of new areas of inflammation as seen on MRI
 - Show some evidence of delaying disease progression and/or disability
- Some may prevent or delay a second clinical attack (relapse) for individuals with clinically isolated syndrome (CIS); CIS refers to individuals who do not meet the criteria to be diagnosed with MS, but have experienced symptoms

The largest unmet need in MS is treatment of the progressive course of the disease. Developing new therapies for progressive MS has been difficult, as the underlying driver in this form of MS remains unclear. Researchers know that inflammation is a part of the disease, but progressive MS is believed to be largely driven by the degeneration of neurons in the brain and spinal cord, which is a complex process. Long-term goals in the development of treatments include turning off the inflammation; however, the major target for preventing progression is to slow or halt neurodegeneration.

Traditional MS clinical trials have been performed for decades with various therapies to treat relapsing forms of MS, and these are typically conducted over a two-year period. The disease process in progressive forms of MS occurs more slowly, over the course of several years, so two-year studies often have trouble adequately measuring progression or determining the effectiveness of a potential treatment.

MS researchers are currently looking at measures of brain volume on MRI and ocular coherence tomography (an imaging technique that provides three-dimensional pictures of the nerves around the eye) as quantifiable measures of progression in MS. These are separate from the changes in symptoms reported by people with MS or neurologic exam findings and disability scores according to EDSS. Currently, the focus of research has switched to early-phase studies using neuroprotective agents to determine if these may alter the course of progression in MS.

Disease-Modifying Therapy to Delay Progression in MS

Disease-modifying therapies (DMTs) that target the progressive course of the disease are desperately needed. In recent years, with the success and inception of multiple new therapies for relapsing MS, the focus is finally shifting to progressive MS. Fortunately, in 2016, successful results of the ORATORIO phase III clinical trial in PPMS studying ocrelizumab, a monoclonal antibody that depletes mature B cells, showed positive results in delaying progression in PPMS, while demonstrating superiority to Rebif® (interferon beta-1a). Ocrelizumab is infused once on day one, a second time on day 14, and then one infusion every six months.

In people with PPMS, ocrelizumab was shown to delay progression of clinical disability (worsening function) at 12 weeks in 24 percent of patients. Given the brand name Ocrevus®, this therapy was approved by the United States Food and Drug Administration (FDA) in March 2017. This therapy also demonstrated significant benefit in two phase III clinical trials in RRMS, OPERA I and II. A prior study, the OLYMPUS trial in PPMS, using a similar agent, Rituxan® (rituximab), did not show benefit in overall prevention of disease progression, but did show benefit in a subset of individuals who were younger than 50 and with active gadolinium-enhancing lesions on MRI (these are lesions with active inflammation). Rituxan has been used off-label in both progressive and relapsing forms of MS, which is a challenge to obtain for many people with MS due to insurance denials. This is related to the lack of an FDA-approved indication for MS at this time.

Prior to the Ocrevus studies, clinical trials in progressive MS with other experimental treatments have been disappointing. Among others, the following agents have been tested in PPMS in phase III clinical trials without benefit in the overall study population: Copaxone® (glatiramer acetate), Rituxan, IV immunoglobulin, Marinol® (dronabinol), and Gilenya® (fingolimod). Additional studies evaluating pulse methylprednisolone IV and other immunosuppressants, including methotrexate, did not delay progression of the disease.

In SPMS, a recent study using an oral therapy that is similar to Gilenya, called siponimod, was shown to have beneficial effects in a phase II clinical trial. As of the time of this publication, siponimod is not FDA-approved for MS. Previously, Novantrone® (mitoxantrone), originally approved in 2000, was FDA-approved in SPMS; however, it has largely fallen out of use due to serious risks of secondary acute myeloid leukemia (AML) and cardiotoxicity (congestive heart failure). Some of the additional agents that have been evaluated in clinical trials and failed to show any benefit in SPMS include: Avonex® (interferon beta-1a), Rebif® (interferon beta-1a), Betaseron® (interferon beta-1b), IV immunoglobulin, cyclophosphamide, myelin basic protein 8298, and linomide.

Currently, many individuals with progressive MS continue on DMTs used to treat relapsing forms of MS. Although not approved by the FDA for this type of MS, these individuals have a perceived benefit from a DMT for MS – even in the secondary-progressive phase of the disease. Their treating neurologists believe that the DMTs approved for RRMS reduce inflammation in all MS, including progressive MS. As always, people with progressive MS are encouraged to discuss treatment options with their neurologist.

Individuals with MS and their families need to understand that current disease-modifying therapies for MS do not restore function, but are used in an effort to slow progression of the disease. Remyelinating and restorative therapies are currently being studied.

Rehabilitation through Physical, Occupational, and Speech Therapy

The medical community embraces the “it takes a village” comprehensive approach to MS care. As such, people with MS can often greatly benefit from working closely with neuro-physical therapists (neuro-PTs), occupational therapists (OTs), and speech pathologists.

Generally speaking, neuro-PTs can help improve one’s ability to walk and remain mobile. PTs often help people with gait, transfers, balance, and coordination, along with stretching and strengthening the muscles of ambulation. Specialized PTs can also assist with more specialized issues, such as those related to the pelvic floor, fitting individuals for custom wheelchairs, and addressing other specific needs requiring individualized attention.

OTs are experts at improving independence with activities of daily living, such as brushing teeth, using the bathroom, and putting on socks. They are experienced in optimizing hand dexterity and function. OTs can also assist with retraining people with MS to drive cars safely with adaptive equipment.

In addition to helping with any speech and communication difficulties one may be experiencing, speech pathologists provide expert assistance to optimize safe swallowing. Speech pathologists also help with improving/maintaining aspects of cognition and memory via “cognitive rehabilitation” training.

Symptom Management

A wide variety of symptoms can occur with progressive forms of MS. A great deal of information on these symptoms and their treatments may be found on MSAA's website at mymsaa.org. To help categorize the effects of MS, MSAA has grouped the commonly experienced symptoms as follows:

Common Physical Symptoms of MS

- balance problems
- bladder dysfunction
- bowel problems
- muscle spasticity (stiffness)
- sexual dysfunction
- speech difficulties
- swallowing disorders
- tremor
- walking and mobility issues

Common Emotional, Mental, and Psychological Symptoms of MS

- anxiety
- cognitive changes
- depression
- Pseudobulbar Affect (PBA)

Common “Invisible” Symptoms of MS

- dizziness/vertigo
- fatigue
- numbness
- pain
- sleep issues
- Uhthoff's syndrome
(the temporary appearance of symptoms resulting from heat stress)
- visual disorders
- weakness



A few of the more impactful symptoms in progressive MS have been highlighted in the sections to follow. However, as noted earlier, details on all of the common MS symptoms, along with treatment options, are available on MSAA's website at mymsaa.org.

Bladder Problems

Bladder dysfunction in MS happens when nerve signals to the bladder and urinary sphincter (the muscles surrounding the opening to the bladder) are blocked or delayed because of MS lesions in the brain and/or spinal cord.

There are basically two major muscles involved in emptying the bladder: the detrusor muscle and the sphincter muscle. As a result of MS, the detrusor muscle in the wall of the bladder involuntarily contracts, increasing the pressure in the bladder and decreasing the volume of urine the bladder can hold. This causes symptoms of going frequently, leaking urine, urgency, or interfering with a good night's sleep.

In other words, the inability to store or hold urine in the bladder occurs when the bladder is unable to retain urine when it accumulates. Instead of expanding when urine collects, the bladder involuntarily contracts, which can make people feel as if they have an urgent need to go to the bathroom much of the time – even when there isn't much urine in the bladder.

The flow of urine is controlled by the sphincter in the bladder, the muscle which relaxes to open and contracts to close. An “inability to empty” means that even though a person senses that his or her bladder is full, the nerve impulse telling the muscle to open is interrupted and never reaches the urinary sphincter, and the sphincter muscle closes before all the urine is emptied from the bladder. When emptying the bladder completely, one might feel the urge to void often but have hesitancy when trying to void. People may also wake up at night often to void since the bladder is not completely empty during the day. Bladder infections or urinary tract infections (UTIs) can occur if urine, which is a waste product, sits in the bladder too long.

Leakage of urine can occur in some cases when the sphincter remains at least partially open, resulting in involuntary leaks. Sometimes the detrusor muscle and the sphincter muscle do not work in coordination and a person with MS can experience many bladder symptoms.

Individuals with MS can experience a variety of bladder issues:

- urinary frequency, which is the need to urinate often; urgency, referring to the sudden urge to urinate; or hesitancy, where an individual has trouble initiating urination
- urinary retention, referring to difficulty emptying the bladder
- urinary incontinence, which is the inability to or difficulty with holding urine
- recurrent urinary tract infections (UTIs)

Treatment options include:

- pelvic floor therapy, using exercises to strengthen pelvic muscles
- using scheduled times to urinate
- avoiding caffeine

- staying well-hydrated until a few hours prior to bedtime
- percutaneous tibial nerve stimulation (PTMS) for overactive bladder, giving electrical stimulation to the ankle, which stimulates sacral nerves that control bladder function
- using medications to treat bladder problems; these include:
 - ▶ Ditropan® and Ditropan XL® (oxybutynin)
 - ▶ Detrol® and Detrol LA® (tolterodine tartrate)
 - ▶ Vesicare® (solifenacin)
 - ▶ Enablex® (darifenacin)
 - ▶ Levsinex® (hyoscyamine)
 - ▶ Flomax® (tamsulosin) and other antihistamines
 - ▶ Hytrin® (terazosin); Minipress® (prazosin)
 - ▶ DDAVP (desmopressin)
 - ▶ Botulinum Toxin (Botox®)
 - ▶ Myrbetriq® (mirabegron)
 - ▶ Sanctura® (trospium chloride)
 - ▶ Tofranil™ (imipramine hydrochloride)
 - ▶ Toviaz® (fesoterodine fumarate)
- intermittent catheterization, where a tube is inserted into the urethra to manually empty the bladder
- InterStim, which is a surgically placed device to help treat overactive bladder, urinary retention, and some forms of bowel dysfunction
- surgical interventions, such as a suprapubic, indwelling catheter

Bladder symptoms can be treated once symptoms are discussed openly with a medical professional and proper assessment is completed. Sharing concerns with a healthcare provider is important. Individuals may need a referral to a urologist to treat bladder symptoms.

Muscle Spasticity

Spasticity is a term used to describe muscle stiffness and muscle spasms that are common in MS and other diseases affecting the brain and spinal cord. Stretching one's limbs, walking, or even bathing can all become difficult. Spasticity can also be incredibly painful.

Spasticity can occur in any limb, but it is the most common in the legs. It can be exaggerated by cold temperatures, infection, fever, recent surgery, or any other harmful stimuli to the body. It may increase with movement or a change in position.

If spasticity is untreated, serious medical problems can occur. These can include pressure sores (ulcers) on the body where pressure occurs. The most common locations for pressure sores are the buttock area, sacral area (at the tip of the spine), on the heels, and other areas that may experience pressure for an extended period of time when sitting or lying still. Untreated spasticity can also lead to contracture, known as frozen joints.

Some degree of spasticity is beneficial, as it can stiffen weak muscles and enable one to stand, walk, or transfer better. Treatment of spasticity focuses on a balance between loosening muscles for comfort, and preventing complications by avoiding complete resolution of spasticity. This balance is needed in order to allow an individual to continue to engage in activities of daily living (ADLs).

Treatments for spasticity are individualized, and may be grouped according to the severity of the symptoms.

For mild to moderate spasticity:

- stretching program
- physical and occupational therapy
- medications used include:
 - Baclofen (formerly available as Lioresal®)
 - Gablofen® (baclofen injection)
 - Zanaflex® tablets and Zanaflex Capsules® (tizanidine hydrochloride)
 - Valium® (diazepam)
 - Klonopin® (clonazepam)
 - Dantrium® (dantrolene sodium)
 - Neurontin® (gabapentin)
 - Tegretol® (carbamazepine)
 - Keppra® (levetiracetam)
 - Requip® (ropinirole)
- botulinum toxin injections for focal (localized) areas of spasticity; these are best for isolated muscles that are stiff; not for widespread spasticity
- Medical marijuana (cannabis) has been used experimentally in treating spasticity and is available by prescription in some states

Therapies for moderate to severe spasticity (the first four listed are also used for mild to moderate spasticity, noted above)

- stretching program
- physical and occupational therapy
- oral muscle relaxers
- botulinum toxin
- intrathecal baclofen; this medication works to relax muscles, and when infused directly into the spinal fluid via an intrathecal pump, it relaxes muscles more effectively and at significantly lower doses, versus the oral form of baclofen (these small doses also avoid the generalized side effects of drowsiness and memory difficulties, which can occur with higher doses of the medication)
- phenol injection; although rarely prescribed, this nerve-blocking agent is sometimes used for severe cases of spasticity
- surgical tendon release; although rarely prescribed, this surgical procedure cuts a tight tendon to relieve pressure

Walking and Mobility Issues

Everyone should have the goal of achieving, and then maintaining, the highest possible level of independent function. This includes safe mobility – both at home and in the community. Ideally, anyone with MS should receive a baseline evaluation from a physical therapist (PT) experienced in MS care. An evaluation can spotlight many subtle symptoms that can be addressed before they worsen into significant issues. These symptoms might include:

- Fatigue/decreased endurance
- Foot drop/drag (especially later in the day)
- Weakness in leg(s) and/or trunk
- Deconditioning
- Mild spasticity (increased tone, which gets worse with fatigue)
- Muscle tightness from inactivity
- Compensatory movement patterns (such as “hiking” or lifting of the hip; leaning to clear the weak leg when walking; or using arms to help stand up)
- Problems with balance (which may include falls, near-falls, and/or difficulty on stairs)
- Impaired vision or sensation
- “Wobbly” walking

All of these problems will affect independent walking and can be targeted in a corrective program. If an individual may benefit from some type of an aid, a physical therapist may have a variety of ambulation aids available to try to see which items work the best.

Understandably, many individuals with MS are initially quite reluctant to accept a walking aid and often delay going to therapy. Individuals with MS should try to view ambulation aids as tools that have the potential to normalize their walking pattern. By doing so, this can result in less fatigue, improved posture and balance, less pain, more endurance, less risk of falling and the correct training of the walking muscles. Dramatic improvement may be seen in an individual's gait and endurance by initially using these aids for training, and later, just as needed for issues such as distance, energy conservation, and worsening symptoms during MS flare-ups.

Many different ambulation tools are on the market, so a professional should be involved in assessing and prescribing those best suited to each person's needs. These include items such as a foot-drop brace, folding cane, lightweight forearm crutches, rolling walkers, and Functional Electrical Stimulation (a wireless technology only appropriate for some). Many wheeled-mobility options are also available for those with limited or no ambulation abilities.

Currently, Ampyra® (dalfampridine) is the only medication approved by the FDA specifically to improve walking speed in individuals with MS. It is an oral, timed-release medication developed to improve the conduction of impulses between damaged nerves of the central nervous system (CNS).

Emotional Issues

Anxiety and depression are more common in MS than in the general population. In fact, more than half of all people with MS will experience these symptoms at some point during their lives. Emotional health is a critical component to successfully managing progressive MS. This includes, when appropriate, the judicious use of antidepressant medications, referrals to trained counselors, and participation in support groups. Additionally, staying physically, intellectually, and socially active all help to promote good emotional health.

Anxiety

Anxiety is perhaps the most taxing and under-treated psychological effect of living with MS. It does not appear to result from the physical disease process of MS, but rather stems from the realities of living with MS. Individuals living with MS know that it's the unpredictability, and therefore the difficulty, in planning and preparing for the effects of MS on life, that drives one's anxiety. Anxiety disorders are estimated to affect 43 percent of those with MS, and are also more common among women.

Anxiety represents a symbolic, perceived threat to one's sense of self, which may be defined as how someone sees him or herself and the unique qualities that he or she possesses. As MS progresses, different challenges and new uncertainties must be faced. This can result in more adjustments, more losses, and more anxiety.

Examples of the physiological symptoms of anxiety include (among others): trembling, increased heart rate or heart palpitations, dry mouth, nausea, tingling in fingers or toes, lightheadedness, insomnia, and more. Examples of the psychological symptoms of anxiety include (among others): chronic unhappiness, frequent worry or guilt, fearfulness, indecisiveness, feelings of inadequacy, repeating certain behaviors or ruminative thoughts (pondering over something repeatedly), excessive concern with physical health, and negative thinking about the future.

Lowering anxiety requires many steps that include learning stress-reduction techniques. Learning to control reactions and quiet oneself can allow someone to feel anxiety when needed to problem-solve, but not to become so overwhelmed by it. Increasing the areas of where you can have control and prioritizing activities can also help. Developing a more spiritual, entrusting attitude has also been found to be helpful to many.

Psychotherapy, either psychodynamic or cognitive/behavioral, includes stress-reduction techniques such as guided imagery, biofeedback (a technique that teaches individuals how to control their body's responses), and meditation. These can be very helpful to reduce anxiety. Medication management is also available. However, options should be discussed with one's doctor, as some medications for depression may worsen anxiety, and some medications may also have the potential for addiction.

Depression

In regard to depression, researchers believe that the high rate of major depressive disorder, dysthymia (a chronic type of depression), and bipolar disorder with MS, is a result of the disease process or the etiology of the disease itself. In other words, the damage to the nerves within certain areas of the brain is believed to increase the chance of greater depressive reactions. Depressive reactions are not to be confused with sadness or fatigue.

In all types of depression, activities of daily living can feel overwhelming and people tend to believe that their feelings will never change. Several symptoms of depression are common ones of MS, such as fatigue, trouble sleeping, cognitive difficulties – especially being unable to focus and concentrate – and feeling slowed down. These similarities can, however, be distinguished by a mental-health specialist who has experience with chronic disease, such as a social worker, psychologist, or psychiatrist, who is specialized or certified in a related area.

For family members, understanding the physical symptoms of MS is often easier than understanding the emotional ones. When depressed, becoming passive, exhibiting a negative mood, and experiencing low motivation are common; some may even withdraw from others. This may irritate family members, causing them to be critical or expecting the person to do one thing to snap out of his or her mood. They may feel at a loss encountering the individual's helpless mood.

If withdrawn, family members may withdraw too, as they may not fully understand what is needed. A loss of sexual interest or libido is also common and this too can have a negative impact on couples. Depression is not overcome by the power of positive thinking. Family members should avoid giving advice. Instead, a referral to a skilled mental-health professional who can work with both the individual and/or family is needed, as well as an evaluation with a psychiatrist to see if specific antidepressant medication would be helpful.

Since individuals with depression experience greater fatigue, withdrawing to try to preserve energy is natural. This can result in not taking one's medication or forgetting to do so, not having the energy to exercise, and less energy to put into relationships and work. A good plan is to focus on a few tasks to accomplish each day to conserve energy, instead of trying to cover all of them. Taking the steps needed to engage social supports and resources is far more difficult when depressed, so having these supports and resources in place beforehand is another vital strategy.

Participating in psychological therapy and taking a medication for depression appear to be the most effective means of treating depression. Treating depression with a medication or a drug alone does not address the underlying causes. This is because communicating and sharing experiences with others and with a mental-health professional has been shown to improve one's ability to cope and to continue to find meaning in one's life.

Many types of psychotherapies may be effective in treating depressive disorders. These include cognitive behavioral therapy (CBT), psychotherapy, problem-focused supportive-group therapy, and telephone-administered CBT for individuals with MS who experience significant levels of depression.

For treatment with medications, consulting a psychiatrist, if possible, may be of greater benefit. Many managed-care and insurance plans have psychiatrists available for medication management. A therapist can also aid in this referral process. Consulting a psychiatrist is important because general practitioners or family physicians may not be as familiar with the range of antidepressant medications available, versus someone who specializes in this field.

Some of the commonly prescribed medications for depression include:

Selective Serotonin Reuptake Inhibitors (SSRI):

- Paxil® (paroxetine)
- Prozac® (fluoxetine)
- Zoloft® (sertraline)
- Lexapro® (escitalopram)
- Celexa® (citalopram)

Selective Serotonin and Norepinephrine Reuptake Inhibitors (SRNI):

- Cymbalta® (duloxetine hydrochloride)
- Serzone® (nefazodone)
- Wellbutrin® (bupropion)
- Remeron® (mirtazapine)

Tricyclic Antidepressants:

- Elavil® (amitriptyline)
- Pamelor® (nortriptyline)
- Tofranil® (imipramine)

Individuals should note that steroid use is known to induce depressive reactions or exacerbate bipolar reactions in individuals. Additional medications, such as those used to treat urinary incontinence or spasticity, can also affect mood. If taking one or more of these medications, individuals are advised to check with their physician to see if these in any way are lowering mood.

For some, an antidepressant, such as certain SSRIs that work on depressive and anxious symptoms, is prescribed. Examples include Celexa® (citalopram) or Lexapro® (escitalopram). Additionally, Effexor® (venlafaxine) or Cymbalta® (duloxetine hydrochloride) may also be considered. Specific anti-anxiety medications like Valium® (diazepam) may work on an as-needed basis, but these tend to have short half-lives. This means that they work only for short periods of time or to aid sleep, but they are not designed for long-term use.

Cognitive Issues



Traditionally, cognitive issues were not believed to be a symptom of MS. In more recent years, researchers and physicians have come to find that roughly half of the MS population will experience some type of change in their cognitive abilities during the course of their disease.

The most commonly affected cognitive processes in MS are

speed-of-information processing, memory, and executive functions (decision making). Other domains of cognition can also be affected depending on where lesions are located. However, rarely are all domains of cognition impacted by MS. Changes in cognitive abilities typically are clinically considered mild-to-moderate in severity, although even mild changes can be annoying and irritating in day-to-day functioning.

Several strategies may be used to help with cognitive problems. These range from avoiding distractions, writing reminders, and asking others to speak clearly, to participating in cognitive rehabilitation, taking medications or supplements (for memory, depression, and/or fatigue), and if appropriate, taking a disease-modifying therapy to slow disease activity. Several books and other resources are available on this topic, although anyone experiencing cognitive changes should first speak with his or her doctor to identify potential causes and appropriate treatment choices.

Fatigue

Fatigue has been described as an “overwhelming sense of tiredness.” Up to 80 percent of people with MS experience the disabling effects of fatigue. This overwhelming tiredness could occur any time in the course of MS, and it has not been shown to be related to measures of disability like the EDSS (Extended Disability Status Scale). Many people with MS find that fatigue increases as the day goes on, and worsens with a rise in body temperature, which might be caused by hot and humid weather.

Many people with MS find that fatigue limits their enjoyment and participation in many activities. Fatigue can make performing tasks on the job or at home difficult. Although researchers do not know at this time what causes fatigue in MS, a number of influences on fatigue have been identified.

Fatigue is complex. Among others, some of the many types of fatigue include:

- motor fatigue, caused by prolonged physical activity
- generalized pathologic fatigue, associated with an underlying medical or psychological condition, such as MS or depression
- cognitive fatigue, where someone experiences reduced attention and slowed thought processing
- heat-induced fatigue, caused by a warm environment or fever

These multifaceted origins involve both central nervous system and peripheral nervous system mechanisms. Since MS may be associated with depression, fatigue, and cognitive dysfunction, treating all of these conditions may create a synergistic effect – referring to a greater effect through the combination of treatments. Other contributing factors can include infection, poor sleep, and sedating medications.

Strategies to help fight or treat fatigue include:

- Reviewing medications that may increase fatigue
- Exercising, which has been shown to significantly reduce fatigue in MS
- Planning activities to avoid triggers and conserve energy; for example, individuals who are heat sensitive can plan ahead to avoid outside activities in the midday sun, as well as make efforts to reduce activity – such as by parking closer to a store entrance to avoid a long walk; a handicapped parking permit can be of help
- Treating depression in MS can sometimes improve aspects of fatigue, which can occur with pseudo-dementia (cognitive dysfunction as a consequence of any underlying depression; may be reversible with antidepressants) and generalized pathological fatigue (caused by the disease)

- The judicious use of prescription stimulant medications can help to pharmacologically combat fatigue in MS, although insurance companies may not always cover these types of medications
- Commonly prescribed medications include:
 - Provigil® (modafinil)
 - Nuvigil® (armodafinil)
 - Symmetrel® (amantidine)
 - Ritalin® (methylphenidate)
 - Dexedrine® (dextroamphetamine)
 - SSRI antidepressants (Prozac®, Paxil®, Zoloft®)

Fatigue can be difficult for family members and friends to understand, because it is invisible to others. If fatigue is poorly understood, a person with MS who is experiencing fatigue might be characterized as “lazy.” Educating family, friends, and partners about MS fatigue is very important.

Neuropathic and Neuromuscular Types of Pain

More than 50 percent of individuals with MS identify pain as a significant symptom. For many years, the medical community did not support the idea that pain could be caused by the effects of MS, but physicians today recognize that pain is a common symptom.

MS pain is mixed and may be divided into two different types. Pain from MS can be a direct result of damage to the nerves (referred to as “axons”) of the central nervous system (CNS), which consists of the brain and spinal cord. This first type of pain is referred to as **neurogenic or neuropathic pain**, and is caused by a lesion in the CNS. This type of pain may be intermittent or steady; spontaneous or evoked. It is often described as numbness, pins and needles, burning, or hypersensitivity.

Non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen usually won’t work well on this type of pain. The over-stimulated nerves need to be calmed, and this may best be accomplished with anti-epileptic drugs, tricyclic antidepressants, and antispasticity drugs, to treat painful spasticity and spasms. Topical medications such as lidocaine gel or Zostrix® (capsaicin topical analgesic) may help reduce the burning and tingling. Optic neuritis is often treated with steroids to reduce the inflammation of the optic nerve. Non-pharmaceutical strategies may help to reduce the perceived severity of the pain.

Treatments include:

- Integrative medical therapies such as acupuncture, hypnosis, cognitive behavioral therapy, mindfulness, and meditation
- Some of the more common neuropathic pain medications include:

- ▶ Neurontin® (gabapentin)
- ▶ Tegretol® (carbamazepine)
- ▶ Keppra® (levetiracetam)
- ▶ Anti-Anxiety Agents (such as Cymbalta®, Valium®, and Klonopin®)
- ▶ Tricyclic Antidepressants (such as Elavil® and Pamelor®)
- ▶ Dilantin® (phenytoin)
- ▶ Lyrica® (pregabalin)
- Capsaicin cream or a lidocaine patch may also be used topically. Additionally, selective serotonin reuptake inhibitors (SSRIs) and selective serotonin and norepinephrine reuptake inhibitors (SRNIs) may be used as well. These specific medications are listed in the section on depression.
- Medical marijuana (cannabis) has been used experimentally in treating pain and is available by prescription in some states.

If taking long-term narcotics, a pain-management specialist may be consulted to address potential addiction, provide psychiatric care, and care for other related issues.

A second type of pain is associated with living with disability and its effects. This is referred to as **nociceptive**. Caused by any mechanism that stimulates a pain response, it can be mechanical, thermal, chemical, or electrical. Examples of this type of pain include musculoskeletal pain, lower-back pain, painful spasms, pain related to urinary-tract infection, pain of pressure sores, and even pain associated with disease-modifying drugs.

Unlike neurogenic pain, neuromuscular pain may respond to NSAIDs, which includes ibuprofen (Advil® and Motrin®). Tylenol® (acetaminophen) may help with this type of discomfort too. Antidepressants are sometimes effective and their function is twofold: they may help to shift the perception of pain, while also elevating one's mood (living with chronic pain is known to increase depression, fatigue, and anxiety). Anti-spasticity medications may be used if spasticity and/or spasms are contributing to one's discomfort.

Non-pharmaceutical approaches include acupuncture, massage, tai chi, yoga, meditation, hydrotherapy, and physical therapy, among others. A physical therapist experienced with MS can be particularly useful in returning balance and good posture back to one's movement. Warm compresses can sometimes loosen a tight muscle or reduce lower back pain, while an ice pack is normally prescribed for a recent muscle injury or injection-site reactions.

MS experts caution their patients about chiropractic care as it can potentially aggravate the nerves of the back and neck. If back pain is severe, tests should be done to see if a pinched nerve, slipped disc, or other structural problem is at fault.

Part III:

Healthy Living with Progressive MS



Avoiding Comorbidities that Drive the Disease Faster

The risk of physical disability in MS is increased when people with MS develop additional medical conditions. For example, two modifiable risk factors for developing comorbidities that can accelerate the disease include **smoking** and **obesity**.

People with MS should not start smoking and should quit smoking if they are using tobacco. It is well known that smoking can lead to heart disease, lung disease, and stroke, but it's important for the MS community to understand that smoking accelerates the course of

MS. Smoking leads to a faster rate of worsening in neurologic function (increasing EDSS score), an increase in bright lesions (those with inflammation) on MRI, and faster rates of brain atrophy (loss of cells).

People with MS are also at an increased risk to gain excessive weight, often because they are limited in their mobility. Carrying extra weight, however, makes walking on shaky legs much harder. Extra weight can also affect other disease outcomes. Therefore, avoiding or treating obesity is an important goal in MS care. Working with registered dietitians, practicing portion control, and other “defensive dieting” behaviors, along with daily exercise, all help these efforts. In addition, surgical procedures, such as gastric banding, have been found to be safe and effective in helping morbidly obese individuals with MS to lose weight.

Avoiding Complications from Progression

Progression and worsening of the neurological status can in some cases lead to severe complications. For individuals who have advanced disease with little mobility, lack of limb movements can result in both contractures – joints that don't bend – and decubitus ulcers, commonly referred to as bed sores. For these reasons, it is imperative that less-mobile individuals are frequently repositioned in their bed or chair, participate in stretching programs to remain limber, and have dependent areas of the body, such as heels, buttocks, and back, visually inspected for sores.

Similarly, individuals with progressive MS may be at risk of urinary retention, which is the incomplete emptying of the bladder, and recurrent urinary tract infections (UTIs). Unchecked, these can potentially develop into severe infection and urosepsis (a potentially severe reaction to a bacterial infection of the urinary tract). To avoid this, individuals with MS should promptly report any urinary concerns, such as foul-smelling urine, burning, or double voiding (when one urinates a second time within minutes of voiding initially). Tests to help diagnose bladder problems include urinalysis and bladder ultrasounds, often available at a doctor's office.

Additionally, progression can at times compromise swallowing and result in aspiration pneumonia, which again risks developing into a severe infection. To avoid this, individuals with MS and families should promptly report any choking or coughing while eating or drinking. Speech pathology assessments and swallowing studies can help diagnose these problems. Speech pathologists can also help patients change the consistency of foods and liquids, as well as adopt various techniques for swallowing more safely.

Individuals with advanced progressive disease are also at risk for other physical, emotional, and psychological issues. Family members and individuals with MS need to discuss any changes or concerns with an MS specialist. This will help to minimize these risks and to provide proper strategies to help cope with the long-term challenges of progressive MS.

Discussing Progression with a Healthcare Provider

Individuals need to follow-up with their neurologist or MS specialist for periodic evaluations. A physician will recommend how often someone should be seen, and this may range from every three months to once per year, based on a person's symptoms and needs.

Individuals should bring a list of their symptoms with them to their appointments. These should include any changes that are noticed in daily life in terms of physical symptoms or changes in memory and cognition. Bringing a list of these symptoms will help to not only ensure that all questions are answered during the visit, but also ensure that no questions are forgotten while speaking to the doctor.

Addressing what can be done to lessen MS symptoms is important. Symptom management has shown significant benefit in improving quality of life. Most symptoms of MS can be lessened with the following treatment strategies: medical treatment; physical, occupational, and/or speech therapy; exercise; counseling; and working with a support team comprised of family, friends, and healthcare providers, as well as religious or spiritual representatives, if appropriate.

Following up with a primary-care physician for regular medical care is also important. By doing so, individuals may avoid developing other medical conditions that can make living with MS more difficult.

Strategies for Wellness with Progressive MS

Exercise

Exercise is key in maintaining function in people with MS. It should be considered as important as other medical interventions for the management of MS. Exercise has shown positive effects on walking speed, endurance, and aerobic capacity in MS. People with MS at almost any level of physical ability can work with a PT and OT to develop an exercise plan that is safe and can help to maintain their current level of functioning.

Exercise has also been demonstrated to lower stress and improve mood, energy, physical health, and overall wellbeing. A combination of a stretching program and aerobic exercise is recommended. Wellness programs are being developed across the country to promote exercise, healthy habits, and overall wellbeing.



Aquatic exercise is a good option for many individuals with MS. Research on individuals with MS suggests that aquatic exercise is effective for improving flexibility and range of motion, cardiovascular endurance, fatigue level, muscle strength, mobility function (including gait and balance), quality of life, and psychological wellbeing. In addition, no exercise study reviewed has identified an increase in relapses or reported any other adverse change in neurologic status.

The aquatic environment offers numerous techniques and options for exercise participation with all levels of physical abilities. Whether someone is interested in a high-level aerobic workout, moderate cardio/strength training, or gentle, slow-moving form, aquatic exercise can be adapted to all levels of MS and provide a wide variety of safe, effective, and enjoyable ways to exercise.



Yoga may be especially beneficial, as it releases muscular tension, improves flexibility and circulation, helps with balance and fatigue, and boosts mental alertness. Yoga is a gentle form of exercise, and since it may help to promote more energy than it requires, some find it to be an ideal exercise for those whose energy is limited from MS. By involving sustained muscle stretches, yoga may help to reduce spasticity by encouraging muscle relaxation. Additionally, because yoga encourages muscle groups to work together, it is thought to help with impaired coordination and balance.

Another good exercise option is **tai chi**. This is a form of martial arts that uses slow movements and deep breathing to promote a type of “moving meditation.” It is a gentle, mind-body exercise designed to rebalance the body’s capacity for healing. Improved flexibility and balance control are among the many benefits of tai chi.

A study was conducted at the Texas Woman’s University in Dallas to determine the effects of tai chi on different factors involved with balance and gait in people with MS. Using several scales to measure the effects of tai chi, participants experienced improvements in balance, endurance, and strength. In addition to a decrease in perception of fatigue, significant improvement was also seen in fatigue severity.

Mindfulness has enormous potential for people with MS, where uncertainty for the future can often lead to increased stress and anxiety. This is a cognitive technique that focuses on teaching people to approach stress and life challenges in a different way. The goal of mindfulness is to teach individuals to stay fully in the present, without added judgment or assumptions about their present or future situations. It was originally developed for people with cancer and chronic pain and has been shown to significantly decrease anxiety, depression, and stress in these and many other conditions.

Individuals are strongly urged to consult their physician prior to the start or change of any exercise program or routine.

Diet

Maintaining good general health is very important for people with MS. A healthy, well-balanced diet can assist in this goal. Different diets have been proposed as treatments, or even cures, for the signs and symptoms of MS. Most all of these diets, however, have not been studied in rigorous, well-controlled clinical trials, and the few that have been studied have yielded mixed or disappointing results. In fact, some special diets might be harmful, due to toxic amounts of certain vitamins or lack of other key nutrients.

For this reason, individuals with MS need to discuss dietary plans with their MS provider before embarking on any given new diet. Although no specific “MS diet” has been universally accepted by the medical community, what and how one eats can make a difference in important issues such as energy level, bladder and bowel function, and overall health. MS specialists often recommend that people with MS consider a low-fat, high-fiber diet, such as that recommended by the American Heart Association.

Several well-known diets are available for individuals with certain goals in mind, such as losing weight, improving health, or reducing the risk of developing other conditions, such as diabetes and heart disease. Doctors agree that eating a healthy diet to promote general wellness and prevent certain other medical conditions could potentially have a positive impact on MS and its symptoms.

Reducing salt intake may also be of benefit to individuals with MS. An array of recent research ranging from molecular studies to animal models and even some preliminary human data, has implicated levels of dietary salt – sodium chloride, or NaCl – as potentially affecting MS outcomes. In one study, higher-salt consumption was associated with increased clinical and MRI disease activity in people with MS. Seventy patients with RRMS were followed over two years, tracking sodium intake. This was in conjunction with clinical and MRI assessment every three-to-six months or at the time of relapse. Researchers found that individuals with high-sodium intake had 3.4-times greater odds of developing a new lesion on MRI, and on average, had eight more T2 lesions on MRI. MS relapse rates were higher among those with high-sodium intake.

The Microbiome and MS

In recent years, researchers have found that interactions between a person’s microbiome and his or her immune cells may contribute to the development and severity of many disease states – including MS. The microbiome refers to the many millions of bacteria that reside in a person’s body, with current research focusing mainly on the bacteria that live in the intestines. Specifically, researchers have hypothesized that imbalances in the number or types of different strains of bacteria could potentially cause the immune system to be inappropriately activated to develop an autoimmune disease. Multiple groups are currently conducting research on the microbiome and its potential connection with MS.

Adjusting to Change

As lifestyle, preferences, and abilities evolve, people often must adapt to these changes. However, learning techniques to help cope with change, and learning new skills to better participate in activities for either work or pleasure, are all part of personal growth and can greatly enhance one's quality of life. In the two sections to follow, guided imagery and vocational rehabilitation are described. These are just two examples of how one can adjust to his or her changing abilities and environment, and enable him or her to discover new ways to continue enjoying a productive and satisfying lifestyle.

Guided Imagery

We often hear about the mind-body connection in regard to our health and wellbeing. Many Western-trained physicians and researchers are discovering that the mind appears to have a powerful influence over one's physical and emotional health, a concept long held by those who practice Eastern Medicine. In recent years, a technique known as guided imagery has been gaining much recognition by individuals, families, care partners, and health professionals.

Research is showing that through guided imagery, biophysical and biochemical changes may take place within the body bringing about physical, emotional, and mental benefits. In general, these types of changes include:

- Mood may be improved, by calming, relaxing, inspiring, and motivating
- Depression and anxiety may be reduced
- Intuition, creativity, and performance may be increased
- Blood pressure may be lowered
- Blood sugar may be reduced
- Immune functioning may be improved
- Surgical wounds may heal more quickly
- Pain and headaches may be lessened
- Negative reactions to medications or treatments may be reduced
- Pre-surgery fears may be lessened

Guided imagery requires a state of deep relaxation, and adds the component of a gentle direction for your sensory images. A healthcare professional trained in the area of guided imagery may use a script to first help you to relax, and then he or she may give you a topic to imagine – such as a favorite place to visit, a loved one you would like to see, or possibly envisioning yourself accomplishing an important goal. In more advanced sessions of guided imagery, patients may learn to imagine specific cellular changes going on in their body to help fight disease, or they may return to a specific traumatic event to recall details and find closure.

Seeing a healthcare professional to participate in guided imagery is just one option; guided imagery dialogues are also available on CD, as well as in books. Some therapists may give guided imagery sessions over the phone or record an individualized CD for a client. Group sessions or workshops for guided imagery are additional options.

Vocational Rehabilitation

Many individuals with MS can benefit greatly from vocational rehabilitation (VR). VR provides a wide range of services to help individuals with disabilities succeed with their work. These services may include:

- vocational guidance and career counseling
- evaluation of rehabilitation potential
- restoration of physical and/or mental skills
- vocational and other training services
- rehabilitative technology, including assistive technology services, assistive technology devices, and rehabilitation engineering
- occupational tools and equipment
- transportation to access other vocational rehabilitation services
- job placement into suitable employment
- financial assistance to cover additional costs incurred during the period of vocational rehabilitation
- personal assistance services, such as a personal care attendant, scribe, reader, and interpreter
- assistance with making the transition from school to work
- guidance in starting a business

According to section 102(a) of the Rehabilitation Act of 1973 (with amendments), to be eligible for state-funded VR services, a person must be able to benefit from VR services in terms of achieving employment, including supported employment (programs to assist individuals with severe disabilities). The person must also:

- have a physical or mental disability which constitutes or results in a substantial impediment to employment
- be able to benefit from VR services in terms of employment
- require VR services to prepare for, enter, engage in, or retain gainful employment

The Rehabilitation Services Administration (RSA) of the federal government oversees the grant programs that fund the VR programs in each state. The services are free of charge. Unfortunately, due to the number of cases, not everyone who is eligible can receive services. Individuals with the most significant disabilities are given a priority over those with less significant disabilities.

A VR counselor works with an individual to set realistic goals and to develop strategies to assist an individual in the workplace or other vocation. As dictated by a person's specific needs, additional professionals may be involved. For example, a speech-language pathologist (SLP) or speech therapist (ST) may be consulted to help solve speech or communication problems that may affect someone's job performance. Several other professionals can be involved to assist in other aspects, such as setting up the office area for easy access, selecting proper furniture and custom-fitting it for the individual, and training to develop specific job skills.

Living Well With Progressive MS

- Follow-up regularly with a neurologist or MS specialist to discuss DMT's and neurological management
- Follow-up regularly with a primary-care physician to discuss medical co-morbidities
- Obtain adequate nutrition through healthy eating
- Exercise
- Learn strategies for stress management
- Avoid cigarette smoke
- Be tested for Vitamin D levels and correct a deficiency if found
- Maintain relationships and reach out for support when needed
- Connect with MS organizations, local MS groups, and/or online communities

Closing Notes

Written by MSAA Chief Medical Consultant Jack Burks, MD

Understanding Progression in MS is a valuable resource for the entire MS community, explaining the latest advances in the understanding of MS progression. As the title implies, the aim of this booklet is to help people with MS and their loved ones to better understand what is happening when progression in MS occurs, and how – at this point in time – it may be best treated.

In March 2017, the MS community welcomed the first disease-modifying therapy (DMT) approved for progressive forms of MS. This newly approved medication is named Ocrevus™ (ocrelizumab) and it was specifically approved for primary-progressive MS (PPMS) and relapsing forms of MS (RMS), which includes secondary-progressive MS (SPMS) with relapses. This FDA approval was very exciting, since prior to this time, approved disease-modifying therapies were only available for relapsing forms of MS.

In spite of the excitement generated by the approval of a medication aimed at reducing disease progression, this is tempered by the fact that a cure for MS has yet to be discovered. No medication at this time can eliminate MS or the many challenges it presents to all members of the MS community. However, resources such as this booklet, which help to explain the importance of long-term treatments, rehabilitation, symptom management, and wellness strategies, can provide the assistance needed to implement a plan that has the potential to attain the best health outcomes possible.

Adherence to an informed treatment plan – from taking medication precisely as prescribed, to timely follow-up appointments with one's team of healthcare professionals, plus employing important strategies for healthy living – are the best recommendations I can provide to the MS community as MSAA's chief medical consultant. For individuals who do not remain adherent to their treatment plan, the potential benefits are lost, so staying current with prescribed medications and wellness strategies is vitally important.

My hope is that anyone experiencing progression in MS may benefit from this informative publication, by helping him or her to better manage the disease and maximize quality of life. I also want to emphasize that the current research in MS progression continues to inspire other scientists to work toward the “next generation” of MS treatments – those that will further reduce the damage caused by MS and restore lost function. I look forward to the many exciting discoveries ahead, with the ultimate goal of ending this very challenging disease.

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