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## Assessment and Management of the Elderly Patient with Multiple Sclerosis

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**Abstract:** Multiple Sclerosis (MS) is a chronic and often disabling disease that is most often diagnosed in young adults. However, due to better diagnostics and improved medical care, patients with MS have a normal life expectancy. This increase in longevity makes for a change in the demographics of the disease, and clinicians must be prepared to meet the special medical and psychosocial needs of the older MS population. Older patients present with increased medical complexity and require a comprehensive and multidisciplinary approach. Understanding the challenges faced by aging MS patients can help the health care professional minimize morbidity and disability associated with this disease.

**Keywords:** multiple sclerosis, aging, disability, disease-modifying agents, pain, fatigue, depression, cognitive impairments, spasticity

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## Introduction

Multiple Sclerosis (MS) is the most common cause of acquired neurological disability in young adults. Historically, it has been seen as a “young patient’s” disease, as 70% of cases are diagnosed between the ages of 20 and 40 years. The exact etiology of the disease is not known, but current theories suggest that MS is an inflammatory autoimmune disorder with a genetic and perhaps an environmental component. Through medical advances in MS treatment made over the past half century, many patients with MS can now be expected to live well into older adulthood, and as a result the demographics of this disease are shifting. The purpose of this review is to provide a summary of assessment, classification, and treatment approaches for managing both the MS disease process and associated conditions, and to discuss these approaches in the context of the aging MS patient.

## An Overview of MS in Aging

The hallmarks of MS are central nervous system (CNS) inflammation, demyelination, axonal degeneration and gliosis which can create a wide array of brain and spinal cord syndromes. While MS is generally considered a chronic progressive illness, the timing and severity of progression is highly variable and somewhat unpredictable. Major clinical manifestations of MS include sensory deficits, weakness, visual disturbances, cognitive impairment, depression, spasticity, ataxia, heat intolerance, fatigue, pain, and bowel and genitourinary dysfunction.

As the patient with MS ages, morbidities and physiological changes associated with the normal aging process interact with MS-related pathology to influence the severity of impairment and disability. Symptoms associated with aging include fatigue, sarcopenia, dynapenia, cognitive decline, and physiological changes affecting the renal, liver and cardiac systems. Older patient with MS have been observed to have a faster rate of disease progression leading to irreversible disability. Symptoms of MS, such as weakness or fatigue, will be compounded by age related changes including muscle atrophy and reduced cardiopulmonary reserve. In addition, older individuals are more sensitive to medication side effects due to decreased ability to distribute and eliminate metabolites. The risks and benefits of medication use in older adults with MS must be

carefully weighed. These synergistic effects of age and neurological illness present a unique challenge for the clinician and patient.<sup>1-4</sup>

## MS Classification

The diagnosis of MS is usually clinical and defined by discrete neurological events separated in time. The McDonald Criteria, which were revised in 2005 and most recently in 2010, combine clinical presentation with findings on MRI that are characteristic of the disease. The new criteria simplify the diagnostic work-up and allow a more rapid diagnosis of MS while maintaining the specificity and/or sensitivity ultimately resulting in the need for fewer MRI studies. Based on the revised criteria, the presence of at least one T2 lesion in at least two of the four locations considered characteristic of MS including periventricular, juxtacortical, infratentorial and spinal cord supports the diagnosis of disseminated in space. To demonstrate the concept of disseminated in space, a single scan that contains both gadolinium-enhancing and non-enhancing lesions in regions typical for MS qualifies to make the diagnosis.<sup>5</sup>

There are four major subtypes of MS that can be characterized by their disease course: relapsing remitting (RRMS), secondary progressive (SPMS), progressive relapsing (PRMS) and primary progressive (PPMS).<sup>2,3,6,7</sup>

RRMS is diagnosed in 85% of patients on initial diagnoses, and overall 55% have this subtype. Initially in the disease, relapses occur with near recovery to baseline and the patient is clinically stable between episodes. However as the disease progresses, there may be residual deficits that accumulate over time. Exacerbations can last days to weeks to months. The longer a patient has MS, the greater the chance that the relapses will be associated with residual deficits and increasing disability.<sup>3,6,7</sup>

SPMS occurs in 30% of patients and is characterized by gradual progression of disability with or without superimposed relapses. If RRMS is left untreated, 50% of patients will develop SPMS in 10 years and 90% in 25 years. Whether this is due to increased burden of disease over time or to decreased ability for the nervous system to repair itself secondary to aging requires further evaluation.<sup>3,6,7</sup>

PPMS is defined by the gradual progression of disability from onset without superimposed relapses.



This form occurs in 10% of the patients and is most likely to have onset at an older age (40–60 years of age) and fewer cognitive changes due to primary involvement of the spinal cord. PRMS is characterized by the gradual accumulation of neurological deficits from initial disease onset with additional intermittent exacerbations.<sup>3,6,7</sup>

Late onset MS (LOMS) classifies patients who are initially diagnosed after age 55. The prevalence is 4.6%–9.4%.<sup>8</sup> These patients typically present with motor impairments, tend to have a more progressive course, and have a worse prognosis.<sup>9</sup> Diagnosing LOMS is a challenge because it requires ruling out other causes of chronic myelopathy, including cerebrospinal vascular syndromes (CVA), hypertension related disorders, compressive myelopathies, primary or secondary vasculitis, metabolic disease, and degenerative and nutritional syndromes. As a result, diagnosis is often delayed due to low clinical suspicion.

## Assessment and Treatment in MS

When providing care for the patient with MS, one must consider treating the disease process, acute exacerbations, and the associated symptoms. Currently there is no cure, but disease modifying agents are available and can prolong independent functioning. The goal of primary treatment is to reduce frequency and severity of exacerbations.

## Treatment with Disease-Modifying Agents

Medications such as interferons and glatiramer acetate, known as disease modifying agents, are used early in patients with RRMS. The four currently available interferons are Betaseron, Avonex, Rebif, and Extavia. They are typically administered via an intramuscular or subcutaneous injection. These medications have been shown to decrease relapse rate. Side effects include flu like symptoms, injection site reaction, elevated liver function tests (LFTs), and an abnormal complete blood count (CBC). In addition, with frequent administration there may be an increased incidence of the development of neutralizing antibodies resulting in reduced efficacy of the medication.<sup>10</sup>

Glatiramer acetate (Copaxane) is made up of four amino acids, which form a collection of random peptides designed to mimic myelin basic protein.

Side effects include injection site reaction and a short-lived post-injection reaction characterized by chest tightness, palpitations, flushing and anxiety.<sup>10</sup>

Mitoxantrone is an anthracenedione, antineoplastic agent that has been approved as therapy in patients with secondary progressive, progressive relapsing and worsening relapsing remitting MS. When used early, it has been shown to decrease the number of relapses and number of enhancing lesions as well as improve the expanded disability status scale.<sup>9</sup> Common side effects include transient leucopenia, elevated LFTs, alopecia, bluish discoloration of urine and urinary tract infections. More serious side effects include cardiac and hematologic toxicity including cardiomyopathy and acute leukemia respectively. Patients using mitoxantrone require close cardiac monitoring including echocardiograms prior to initiating therapy, before administering each subsequent dose and yearly after completing course of treatment. Patients should also be followed by serial complete blood counts looking mainly at the white blood cells prior and following each dose. Side effects are dose related and should not exceed 140 mg/m<sup>2</sup>.<sup>11</sup>

Natalizumab (NTZ) (Tysabri), a humanized monoclonal antibody, which binds to the alpha-4 beta1 integrins on leukocytes, reduces inflammation in the nervous system by preventing leukocytes from crossing the blood brain barrier. It is used for treating relapsing multiple sclerosis in patients with an inadequate response to, or cannot tolerate other therapies. It has been shown to reduce the risk of disability progression and decrease the annual relapse rate. However, most studies looking at NTZ as monotherapy or in addition to interferon beta-1a were done in patients <55 years old. NTZ was initially approved in 2004, but was withdrawn in February 2005 secondary to ten reported cases of progressive multifocal leukoencephalopathy (a viral infection of the brain that usually leads to death or severe disability). However, after safety evaluation, it was reapproved by the FDA in 2006. Due to the risk of these dangerous side effects, the medication can only be given through a special distribution program called the TOUCH™ Prescribing Program. Other adverse reactions include liver damage, allergic reaction, fatigue, headaches and infections.<sup>12</sup> The efficacy, tolerability and safety of NTZ was recently looked at in a Cochrane review which demonstrated decreased



risk of exacerbations and progression of disease over two years with good tolerability. Side effects include infusion reactions, anxiety, sinus congestion, lower limb swelling, rigors, vaginal inflammation and menstrual disorders.<sup>13</sup>

Fingolimod (Gilenya) is a novel medication that has recently received FDA approval and is currently being used as first line treatment of relapsing-remitting and primary progressive MS. It is an oral sphingosine-1-phosphate receptor modulator aimed at inhibiting lymphocytes from leaving secondary lymphoid organs thereby preventing them from attacking myelin. It may also have neuroprotective and reparative effects as well. It has been shown to decrease relapse rate as well as disease activity. It is an oral preparation and therefore older patients that may have difficulty with injections can take it with ease leading to improved compliance. First dose side effects include bradycardia, which peaks 6 hours after dosing requiring close monitoring after initial dose and symptomatic management. Other first dose side effects include headache, influenza, diarrhea, back pain, liver abnormalities and cough. Long-term side effects include increased risk of infection, macular edema, decreased pulmonary function and hepatotoxicity.<sup>14,15</sup>

Azathioprine (Imuran) and Cyclophosphamide (Cytoxan) are both immunosuppressants used to slow down the demyelinating process. The use of azathioprine as a treatment for MS remains controversial in light of mixed research results. Side effects include nausea, anemia, leukopenia, liver damage, and a long-term increased risk of developing cancers such as leukemia or lymphoma. This medication is less likely to be tolerated in an older population and if used may require long term monitoring for cancers. Cyclophosphamide has shown only a modest benefit. It appears to be most effective in patients younger than age 40 years, especially in those who have been in the progressive phase for less than one year. The duration of treatment is limited by the risk of bladder cancer, which appears to rise with time and may depend upon the total accumulated drug dose.<sup>10,16</sup>

## Evaluation of the Older Patient

When evaluating older MS patients for treatment, it is important to determine if new symptoms represent progression or exacerbation of the underlying

disease or a separate underlying disease process. This poses a unique challenge for the clinician, as these symptoms often overlap. It is important to have a high index of clinical suspicion and to order the appropriate diagnostic tests in order to diagnose and appropriately treat the underlying condition. For example, consider an aging patient with MS who presents reporting subjective declines in cognitive functioning (in terms of mental processing speed and word finding) as well as increases in spasticity and fatigue. These symptoms could represent MS disease progression, or could instead be related to “aging” concerns such as cerebrovascular changes, decreases in sleep efficiency (perhaps secondary to apnea) and declines in overall respiratory fitness. Likely, such symptoms reflect an interaction of MS and normative aging processes, and separating such features diagnostically may prove impossible. However, as always it is important to take a detailed history to decipher the source of the symptoms and to target treatments. A functional history is important to determine how the disease process as well as the aging may be affecting patient’s activities of daily living and mobility.

## Disease Modifying Agents in Older Adults

Most studies that have evaluated these disease-modifying agents have studied patients with a mean age of 34–47, and have followed these patients for only a few years. Very little work has examined the effects of these medications on an aging population, and more studies are needed to confirm long term safety, efficacy and tolerability. For example, immunosuppressants are mainly used for progressive MS, but in the older population, the risks including medication side effects, cardiac toxicity and increased risk for infection may outweigh the benefits.

## Treatment of Secondary Symptoms in MS

MS is associated with a number of debilitating symptoms, including pain, fatigue, depression and cognitive dysfunction. These symptoms can have a significant negative impact on quality of life, and can limit one’s ability to continue to participate in an aggressive rehabilitation program.



## Pain

Pain is one of the most common symptoms of MS and can be seen in more than half of all patients with MS. Pain can either be neuropathic or nociceptive. Patients with MS may experience trigeminal neuralgia, electric shock sensation radiating down the spine or into limbs with neck flexion (Lhermitte's sign), dysesthetic pain, back pain, visceral pain and pain secondary to muscle spasms.<sup>17</sup> In the older population, these pain conditions may interact with other pain sources associated with normative aging (eg, osteoarthritis, diabetic neuropathy). The initial evaluation should determine if there is a physiologic or structural reason for the pain that can be corrected. Etiologies such as cervical and lumbar spondylosis may occur in conjunction with MS, and MRI of the cervical or lumbar spine should be part of the diagnostic work-up.<sup>18</sup>

Studies have shown that both MS patients and older adults are often under-treated for pain, which can result in increased morbidity.<sup>19–21</sup> Medications useful for treating pain in this population includes opioid analgesics, nonsteroidal anti-inflammatory drugs (NSAIDS), anti-seizure medication, antidepressants anti-spasticity agents, and cannabinoids. An intrathecal pump may also be beneficial for pain secondary to spasticity. In older adults, side effects of opioid class medications include constipation, respiratory depression, confusion, and lethargy. As a result, these analgesics must be prescribed and monitored with care, and dose adjustments may be necessary. The NSAIDS should be used with caution in the elderly due to the increase risk of hypertension, myocardial infarction, stroke, gastrointestinal bleeding, and renal insufficiency.<sup>22</sup> Carbamazepine and other anticonvulsants may also increase confusion and ataxia in the elderly. Tricyclic antidepressants (TCAs) or other medications with anticholinergic effects may lead to urinary retention, confusion, cardiac symptoms and autonomic instability.

Much recent evidence emphasizes the importance of a comprehensive, biopsychosocial model for treating chronic pain. In addition to the medication management approaches described above, a number of psychosocial interventions exist and have shown promising efficacy as adjunctive treatments for chronic pain management. These include Cognitive-Behavioral and Operant based psychological interventions<sup>23</sup> as well as relaxation and

self-hypnosis training.<sup>24</sup> Generally, these approaches teach patients to monitor their bodies for signs of stress, to engage in deep breathing and other stress management approaches, to evaluate their thoughts and beliefs about pain, to challenge those thoughts that are deemed alarming or not helpful (eg, catastrophizing cognitions) and to develop and reinforce thoughts that will contribute to better outcomes. A recent meta-analysis of Cognitive-Behavioral trials in chronic pain populations found this intervention to be more efficacious than wait list control conditions for decreasing difficulties with mood and interference with social role functioning, as well as increasing positive cognitive coping and activity level. Cognitive-behavioral treatments were also found to have a significant effect on reducing subjective pain experience and overt pain behaviors as compared to active treatment control conditions.<sup>23</sup> In theory, such approaches may be especially useful in older adults, where side effects of medications make purely pharmacological intervention impractical.

Only a handful of studies have evaluated non-pharmacological pain interventions in MS populations. In one recent pilot study of a cognitive restructuring plus self-hypnosis training program in adults with MS,<sup>25</sup> 15 patients received 16 individual treatment sessions. On average, daily pain intensity was reduced 47% (from an average of 3.0 to 1.6 on a 0–10 numeric rating scale). Participants in this study were on average 52.6 years of age, and no participant was older than 65. There are to our knowledge no trials of psychosocial interventions specifically tailored for older adults with MS-related chronic pain.

## Fatigue

Another predominant symptom in MS is fatigue. Fatigue is present in two thirds of patients with one half describing fatigue as the most disabling symptom.<sup>26</sup> Patients may refer to a “physical” or “mental” fatigue. Common features of MS fatigue include malaise, motor weakness during sustained activity, and difficulty maintaining concentration. Again, a comprehensive assessment is required—an aging MS patient who complains of fatigue should be evaluated to rule out other potential causes, including infection, cancer, anemia, hypothyroidism, rheumatological disorders, sleep apnea and diseases of the cardiovascular, pulmonary, renal or



hepatic system. Medications that can contribute to fatigue include tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), benzodiazepines, opioids, anticonvulsants, beta-blockers, interferons, and antispasticity medications. Other factors that can lead to fatigue include depression, pain, physical deconditioning, disrupted sleep secondary to neurogenic bladder, and exposure to a heated environment.

Once other causes have been ruled out, treatment of fatigue includes energy conservation, initiation of a regular exercise program, and (potentially) stimulant medication. Aerobic exercises have in particular have been shown to be beneficial in reducing fatigue.<sup>27</sup> Medications include amantadine, modafinil and methylphenidate to improve arousal. Caution is required when prescribing stimulants in older patients due to poorer liver clearance and increased risk of cardiac and cognitive side effects. Methylphenidate has been associated with increased heart rate, but has been shown to be safe and effective when looked at adult populations with traumatic brain injuries.<sup>28</sup> Amantadine has been associated with an increased risk of confusion and edema in the elderly.<sup>26,29</sup>

## Depression

Depression is the most common mood disorder in MS, and affects more than half of all patients. Incidence of depression in MS is three times higher than the general population. Depressed affect may certainly be associated with increasing disability and restriction of valued activities, but it is also likely that depression in MS has an organic etiology related to neural disruption. This observation is supported by the fact that depression is more common in MS even as compared to other disabling chronic disease states.<sup>30</sup> Depression may be overlooked, as there are symptoms common to both such as fatigue, reduced activity, decreased appetite, and poor concentration. MS is associated with a 7.5 times higher suicide rate than in the general population that cannot be explained fully by a reactive depression.<sup>31</sup> Duration of MS, severity of physical disability, and cognitive impairment do not appear to affect the risk of suicide.<sup>19,30–32</sup>

Depression may present differently in older adults with MS. Generally speaking, rates of clinical depression tend to decrease with age.<sup>33</sup> Prevalence rates are 1%–3% in the general elderly population and

from 5%–17% in primary medical care settings.<sup>34–37</sup> Nevertheless, older adults are more likely than younger adults to report subclinical symptoms of depression (about 16% in the community),<sup>33</sup> or 29% in primary care settings. When older adults do become depressed, prognosis and impairment are worse compared to younger persons. Studies have demonstrated overall functioning that is comparable or worse than that of people with heart and lung disease, diabetes, and other serious chronic conditions.<sup>38</sup> Older patients may also present with a cluster of symptoms including anhedonia, lack of energy, and poor appetite, but little description of tearfulness or overt sadness.<sup>39</sup> This presentation has been called “depletion syndrome” and “nondysphoric depression”.<sup>40</sup> Among clinically depressed older adults undergoing treatment as usual, at 24 months 33% are well, 33% remain depressed, and 21% are deceased.<sup>41</sup>

There are only a handful of studies of depression in older adults with MS. Results generally reflect findings from non-disabled populations—that is, older adults with MS are at less risk of clinically significant depression than are younger adults with MS, but rates remain higher than in the general population.<sup>42,43</sup>

Treatment options for depression in older adults include medication (generally, the SSRI class is first line, and Citalopram has shown good safety and tolerability in older persons) and psychotherapy (with greatest efficacy being demonstrated by cognitive-behavioral and interpersonal therapy approaches). Behavioral activation, engagement in pleasurable activities, and physical activity are also key in promoting a stable. Referral to a Rehabilitation Psychologist is indicated if a patient fails to respond to antidepressant medication, or more generally if they request assistance with adjustment to disability.

## Cognitive Impairment

Cognitive dysfunction can be seen in up to 50% of patients with MS due to effects on the brain. Changes in cognitive ability can significantly impair one's ability to work and live independently. Although mild cognitive dysfunction occurs frequently, only 5%–10% of patients will develop a severe cognitive dysfunction.<sup>19</sup> Common cognitive deficits include problems in new memory acquisition and recall (often experienced as a “loss of short-term memory”), difficulties with abstract reasoning, word finding, and



certain visuospatial functions, and slowness in the speed of information processing information. General fund of knowledge and receptive language skills are generally unaffected. Decreased short-term memory is the most common finding. Patients demonstrate slowed retrieval of formed memories and often require cueing. Aging itself causes homogeneous cortical cell loss and some structural changes in the frontal cortical-subcortical pathways, which can lead to a slower learning rate and difficulty with memory. Thus, the aging MS patient may be at an even greater risk for significant cognitive disturbance.

The mini-mental examination may be useful in tracking changes in cognition but it may be insensitive to detect subtle cognitive changes occurring in most MS patients. Full neuropsychological assessment is indicated whenever possible to establish a baseline and to monitor for long-term changes.

Additionally, medications should be assessed for possible impact on cognitive function. Medications that can contribute to cognitive slowing, especially in the aging population, include anticholinergics, antispasmodics, opioids, benzodiazepines, and TCAS. Consideration should be given to change to long acting anticholinergics preparations for bladder dysfunction. The use of intrathecal medications or botulinum toxin injections may be used to reduce high doses of oral antispasticity agents. As always, it is important to monitor for signs of depression, anxiety, or fatigue, which may exacerbate cognitive difficulties.<sup>44-50</sup>

To manage cognitive changes associated with MS, patients should be encouraged to use lists, daily journals, and appointment books for activities. Whenever possible, patients should also be seen by a speech therapist or rehabilitation psychologist for training in compensatory cognitive strategies.

## Spasticity

MS patients also suffer due to spasticity and increased tone seen with upper motor neuron lesions. The presence of spasticity can lead to significant pain, impairments in function, and problems with hygiene and positioning. Energy requirement for an activity is increased with the presence of spasticity. In the older patient, rule outs for increased spasticity include secondary causes such as infections, skin breakdown, or spinal stenosis with myelopathy. Oral anti-spasticity medication may be poorly tolerated by

the older population and should be monitored closely. Baclofen use in an elderly patient will require an initial lower dose and a slower titration to decrease the risk of sedation and confusion. Tizanidine should also be used with caution in the elderly since clearance of the drug is decreased four-fold. Monitoring for hypotension and sedation is essential. The benzodiazepines are traditionally poorly tolerated in the older population and are associated with an increased half-life and a higher association of paradoxical reactions, agitation, and disequilibrium. An intrathecal baclofen pump may be useful in patients with primarily lower extremity spasticity.<sup>19,51</sup>

## Treatment of Functional Limitations in MS

Gait disturbances due to muscle weakness, ataxia, sensory loss and spasticity can result in impaired mobility and increased risk for falls.<sup>19</sup> Assistive mobility devices, including canes, crutches, walkers, scooter, and manual or motorized wheelchairs should be considered early to assist with mobility and functional independence. A rolling walker helps to conserve energy, and the addition of hand brakes, a seat, and a basket can be beneficial. It is important to educate each patient on their needs and how to utilize the assist device properly. As patients age, their requirements may change and therefore a falls assessment and mobility assessment should be performed at each encounter.

Orthotics such as an ankle foot orthosis (AFO) may be helpful in improving toe clearance in patients with dorsiflexion weakness. The ground force reaction AFO can add knee stability without much additional weight. Orthotics with high-energy demands such as the hip-knee-ankle-foot orthosis should be avoided, especially in the elderly MS patient. Wrist hand orthosis are useful in the treatment of upper extremity paresis and spasticity. Other equipment that may be required for safety or for energy conservation include bathtub benches, shower chairs grab bars, hoist lifts and stair lifts.

The use of even light weight self-propelled wheelchairs can be difficult for MS patients, especially as they age, and consideration should be given for a motorized wheelchair. Before prescribing a motorized wheelchair, the patient should be evaluated for deficits in cognition, vision, and manual dexterity which



can impair their ability to safely operate the device. The safety of these devices needs to be reassessed periodically as the disease progresses. Patients may prefer a scooter to a motorized wheelchair, as there is less associated perception of disability. However, a scooter is not designed for prolonged seating and a wheelchair will be more useful for those patients who rely solely on motorized devices for mobility. Patients with MS who have risk factors for a progressive course should be compassionately advised to consider wheelchair/handicap accessible housing as early as possible.<sup>52</sup>

Corticospinal tract involvement is present in 62% of patients with progressive disease. Typically patients present with weakness, affecting the lower extremities manifested by foot drop. To improve ambulation, assistive devices such as canes and walkers as well as orthotics can be used. Functional electrical stimulation devices such as the Bioness L300 or Walk Aide have been shown to improve walking performance and may even have long lasting effects due to neuroplastic changes.<sup>11</sup>

A number of medications are aimed at treating functional mobility deficits associated with MS. Dalfapridine (Ampyra) is a potassium channel blocker that has showed promise in improving ambulation in patients with walking disability due to MS. It was approved in January 2010. A phase three, placebo controlled trial looked at 237 patients from 39 centers in the US and Canada aged 18–70 years with clinically defined MS. They found that patients on the dalfampridine showed a 25% improvement in walking speed based on the 25 foot walk test and the drug was well tolerated. Adverse events seen in safety and tolerability studies included ataxia, convulsions, headache, chest pain and seizures.<sup>53</sup>

In addition to medications, rehabilitation strategies including physical therapy and exercise continue to play an important role in the treatment of MS. The primary goal is to maintain strength, mobility, balance, range of motion and functional independence. Exercise and core stability training have been shown to help maintain balance and mobility in patients with MS.<sup>5</sup> Furthermore, exercise can help counteract the effects of disuse atrophy.

Given the potential implications of serious falls, many older patients may develop a “fear of falling” that can actually lead to restriction

of activities, decreased exercise, and behavioral disengagement. This, paradoxically, can contribute to general deconditioning and greater fall risk. A comprehensive team based approach involving joint sessions with a physical or occupational therapist and a psychologist has been shown effective in managing anxiety around falls and associated restriction of activities.

## Treatment of Comorbid Health Conditions

As the patient with MS ages, they should always be screened and evaluated for secondary conditions and co-morbidities that are more common among the elderly, including osteoporosis, osteoarthritis, diabetes, cardiac disease, and cancer. Patients with MS are at increased risk for osteoporosis due to the use of corticosteroids, progressive immobility, vitamin D deficiency and age related bone changes. This loss of bone density, combined with an increased fall risk (due to muscle weakness, sensory deficits, poor balance, and cognitive and visual disturbances) likely contributes to a higher frequency of bone fractures. In a USA MS registry, 27.2% of responders reported a low bone mass and 15% reported history of a fracture.<sup>53</sup> Hip bone mineral density is more affected than vertebral bone mineral density in patients with MS. There are currently no clinical guidelines in the evaluation, prevention and treatment of osteoporosis in MS patients.<sup>53</sup> The current recommendations of screening the general population for osteoporosis includes bone densitometry at the age of 65 for women and 70 for men. However in the MS population, screening should occur sooner if the patient has been on equivalent doses of prednisone 5 mg for greater than three months or scores > 6 on the Expanded Disability Status Scale (EDSS) as this is associated with decreased bone mineral density and increased risk of falls.<sup>53</sup>

Diabetes mellitus type 2 has been shown to be more prevalent in the MS population compared to the general population.<sup>54</sup> Possible explanations for this include muscle disease from nerve demyelination, sedentary lifestyle, obesity and use of glucocorticoids as treatment. Regular monitoring of fasting blood glucose and hemoglobin A1C is indicated in older MS patients. Chronic problems associated with diabetes include microvascular complications such as neuropathy, nephropathy and retinopathy, as well



as CVA and CAD. Many symptoms of diabetes can overlap or mimic symptoms of MS. For example, the neuropathy of diabetes consists of pain and paresthesias beginning distally and spreading proximally in a typical glove and stocking distribution. Also, retinopathy can lead to visual disturbances such as blurry vision, which are also seen in optic neuritis. In patients who have MS and diabetes, treating an acute exacerbation may pose a challenge secondary to the negative effects high dose steroids have on glycemic control. In this case very close monitoring and medication adjustment is essential.

Osteoarthritis (OA) is common among patients over 55 and a majority of patients over the age of 70 have some evidence of disease. Joints including the knees, hips, spine, and hands are subject to degenerative changes secondary to overuse and added stress. Symptoms include pain, joint stiffness, and limited range of motion all of which might reduce functional mobility. Patients with MS may be at increased risk for osteoarthritis because of additional stress placed on joints secondary to weakness and spasticity. Most cases of OA may be treated with conservative methods including physical therapy, NSAIDS, intra-articular steroids and/or viscosupplementation.

In some cases OA may warrant surgical intervention. In the MS population, post-operatively, patients have been found to develop hamstring spasticity, which can lead to a flexion deformity, resulting in pain and decreased range of motion. This may require additional therapy, bracing, muscle relaxants, or subsequent surgery to perform hamstring release. Also, it is important to realize that both general and regional anesthesia have been implicated in MS relapses and should be considered when deciding whether to pursue surgical options.<sup>55</sup>

Cancer is currently the second leading cause of mortality in the US. In 2009, it is estimated that there will be 1.5 million new cases of cancer diagnosed.<sup>56</sup> According to new studies, patients with MS have a decreased overall cancer risk, however they are at a higher risk for developing CNS or urological tumors. The lower rates of digestive, respiratory, prostate and ovarian cancer in MS patients may be secondary to lifestyle changes associated with their illness, immunological changes due to disease activity or treatment effects. There has been some evidence of an increased breast cancer risk in women with MS treated with

immunosuppressive therapy, but this is still under investigation.<sup>57,58</sup> The increased risk for bladder cancer may result from chronic bladder inflammation in the setting of urological dysfunction.<sup>57</sup>

There is an increased risk of brain cancer in MS patients, presumably due to the chronic neurologic inflammation that accompanies the disease. However, patients with MS are imaged frequently and the increased risk may reflect an increase in detection.

Although patients with MS may have a lower risk of cancer than the general population, they still require general screening tests such as annual mammograms for women over 40 (with no risk factors), colonoscopy or flexible sigmoidoscopy in men and women after 50, and prostate specific antigen (PSA) levels in men over 50.

## Conclusion

MS is a chronic, progressive neurological disease that contributes to significant morbidity and disability. Modern disease modifying approaches mean that most patients with MS are expected to live a normal lifespan. This, in conjunction with a general “graying” of the US population, means that the demographics of the MS patient are shifting. MS may typically present in young adulthood, but it can no longer be seen as a “young patient’s” disease. As the patient with MS ages, medical complexity increases. It becomes both more important—and more difficult—to differentiate between exacerbations, progression of the disease, normal physiological aging and disease processes associated with the elderly. Initiating proper diagnostic workup and evaluation along with appropriate treatment strategies are essential to improve quality of life. Although studies looking at older patients with MS are becoming more prevalent, much more research is needed, especially regarding the long term effects disease modifying agents and medications for symptom management. Although there is no current cure for MS, the medical team can play a key role in helping the patient and family adapt to this illness and maintain quality of life.

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