Mobility Concerns in Multiple Sclerosis—Studies and Surveys on US Patient Populations of Relevance to Nurses

Jong-mi Lee, NP[1] and Jeffrey Dunn, MD[2]

1. Nurse Practitioner; 2. Neurologist, Stanford Multiple Sclerosis Center, Department of Neurology and Neurological Sciences, Stanford University Medical Center, Stanford, California, US

Abstract

Despite significant advances in treatments and therapies for multiple sclerosis (MS) over the last two decades, there remains no effective treatment that can definitively halt the progression of functional impairments in MS. Impaired mobility, walking in particular, has been observed in early MS disease, and cross-sectional surveys according to MS clinical criteria have shown that approximately 50 % of existing patient populations with MS require mobility support, such as wheelchairs or walking aids, some or all of the time. Loss of mobility is one of the most disabling effects of MS, and adversely affects independence, employment, and quality of life. Additionally, as patients experience mobility loss, their ability to perform activities of daily living (ADL) decreases and dependence on the assistance of others increases. The stress and physical burden of caring for a friend or relative with MS may affect the health of caregivers and increase their own requirement for healthcare resources. The identification of therapeutic options for improving impaired mobility and coping with disability represents an important aspect of patient management. This review will discuss current published literature on mobility matters in MS, how they affect the patient, and how they are measured and treated, with inclusion of the perspective of a MS nurse specialist.

Keywords

Multiple sclerosis, impaired mobility, assessment, therapeutic options for mobility, nurse practitioners, caregivers

Disclosure: Jong-Mi Lee, NP, has served on nursing advisory boards for Biogen Idec, Teva Neuroscience, and Genzyme. Jeffrey Dunn, MD, has a patent pending for a biomarker to predict treatment response in multiple sclerosis (MS). He has received grant support for clinical research from the Accelerated Cure Project, Genzyme, Roche/Genentech, and Actelion. He has served on scientific advisory boards for Biogen Idec, Teva Neuroscience, and Genzyme. He has received honoraria from the National MS Society and from PRIME® Continuing Medical Education.

Acknowledgments: Editorial assistance was provided by James Gilbart at Touch Medical Media.

Received: May 31, 2013 **Accepted**: July 22, 2013 **Citation**: *US Neurology*, 2013;9(1):17–23 *DOI: 10.17925/USN.2013.09.01.17*

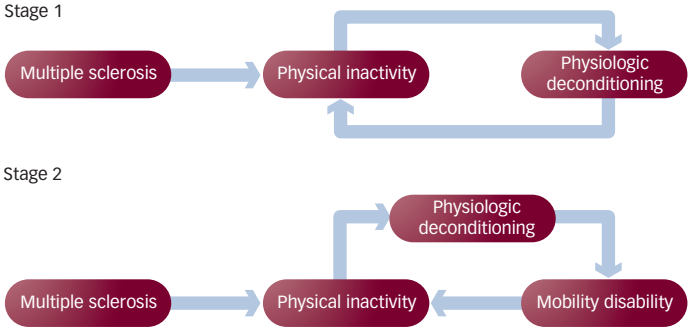
Correspondence: Jeffrey Dunn, MD, Stanford Multiple Sclerosis Center, Department of Neurology and Neurological Sciences, Stanford University Medical Center, Stanford, CA 94305-5235, US. E: jeffdunn@stanford.edu

Support: The publication of this article was funded by Acorda. The views and opinions expressed are those of the authors and not necessarily those of Acorda.

Multiple sclerosis (MS) is a chronic inflammatory-demyelinating disease caused by intermittent and recurrent episodes of multifocal inflammation in the central nervous system (CNS), which results in the demyelination and transection of axons in the brain, optic nerve, and spinal cord. This damage to the neuronal pathways affects signal conduction, causing neurologic disabilities, such as vision problems, difficulty walking, weakness, imbalance, sensory loss, pain, cognitive changes, spasticity, and bladder or bowel dysfunction.[1] MS affects approximately 2.5 million people worldwide,[2] with the majority of people diagnosed between the ages of 20 and 50.[3] Women are more often affected by MS than men, and it is more prevalent in people of northern European descent than in those of other ancestries.[3] In many people with MS, mobility is affected early in the disease, even when clinical measures of disability are minimally altered.[4]

Mobility is defined by the International Classification of Functioning, Disability, and Health (ICF) as "… moving by changing body position or location or by transferring from one place to another by carrying, moving, or manipulating objects, by walking, running or climbing, and by using various forms of transportation …" It has been estimated that 80 % of people with MS (as defined by a previous version of the McDonald diagnostic criteria of 2005)[5] will experience impaired mobility to some degree, within 10–15 years of their initial diagnosis[6] although this figure is decreasing with the widespread use of disease-modifying therapies (DMTs) that delay disability progression. Difficulty with walking is the primary factor contributing to loss of mobility in MS, is often the most visible sign of MS,[7,8] and constitutes one of the most feared and disabling neuromuscular deficits associated with the disease.[8–10] Walking impairment represents a particular concern of those living with

Figure 1: Perpetuating Cycle of Physical Inactivity as a Consequence of Multiple Sclerosis Leading to Mobility, Disability, and Continued Inactivity



Reprinted with permission from Motl et al.[43]

this disease, as continued impairment increases physical inactivity in a positive feedback loop (see *Figure 1*). Loss of mobility in people with MS adversely affects independence, employment, and quality of life (QoL). In this article, we will examine mobility concerns in MS, discuss how they affect patients and their caregivers, and how they are measured and treated. Additionally, we will review the main experiences of mobility and walking concerns provided by a MS nurse practitioner and a neurologist, and briefly examine current and future improvements and developments in the management of people with MS that may reduce the impact of reduced mobility.

Impact of Impaired Mobility on People with Multiple Sclerosis and their Caregivers

Regardless of disability level or disease duration, maintaining mobility is ranked as one of the highest priorities among people with MS,[8] and as the most concerning aspect of the disease.[11] Impaired mobility is closely associated with low self-reported QoL in people with MS, and can profoundly affect the ability of individuals to live independently.[12] In a recent study evaluating the prevalence, severity, and burden of walking and mobility problems (WMPs) in five European countries, WMPs were regarded as the most bothersome MS symptom by almost half of patients (43 %) of the 683 who responded.[7] Multiple studies have reported a correlation between impaired mobility and reduced activities of daily living (ADL), reduced participation in life tasks and community, and decreased QoL.[13–18]

The impact of mobility impairment on daily life is substantial, with walking difficulties reported in 79 % of people with MS in the US.[19] One longitudinal study estimated that by 15 years post MS diagnosis, there is an approximately 40 % probability of a patient with MS needing some type of walking aid and a 25 % probability of them needing a wheelchair.[20] In this study the cohort was defined using the Poser criteria;[21] using the more recently revised 2010 McDonald criteria,[22] the numbers diagnosed would have been greater than the earlier diagnostic potential and applicability to wider populations of the later revisions. In a more recent survey of 703 community-dwelling, working-age adults with MS, 60.5 % were found to own at least one mobility aid, most commonly manual wheelchairs (38.4 %), followed by canes or crutches (35.7 %).[23] People with MS often have difficulty continuing to work, and lost income due to loss of employment or early retirement is the largest single factor contributing to the economic cost of MS.[24] In a recent survey involving 8,681 participants from 125 countries, fatigue (85 %) and mobility factors (72 %) were reported as the symptoms most detrimental to their ability to remain in work.[25] The impact of impaired mobility on employment is marked,[26] correlating with decreased instrumental ADL (IADL) scores, decreased employment, and decreased income. Moreover, an online survey of 1,011 people with MS found that only 34 % who had difficulty walking were employed.[27]

The Expanded Disability Status Scale (EDSS) is the primary disease-specific health measure for MS,[28] and is heavily weighted toward mobility.[29] EDSS scores of 4.0 (severe disability in one of the functional systems but able to walk more than 500 m without aid or rest) and 6.0 (ability to walk with stick, crutch, or other aid no more than 100 m without rest) represent the onset and progression of significant mobility limitations.[30,31] A European study by Kobelt et al. found that, among patients with EDSS scores of 0–1.0, about 70–80 % of those aged 65 years or below were employed.[24,32] For patients with EDSS scores of 4.0, employment varied between countries from 40–76 %; however, for patients with EDSS scores of 6.0, the proportion employed was much lower ranging from 17–44 %.[24] Similarly, in a Canadian study of unemployment determinants among people with MS, participants who were unemployed had significantly more walking limitations than those in employment.[33] Mobility limitations were frequently cited as the reason for unemployment in this study. As patients experience mobility loss, their ability to perform ADL decreases and dependence upon the assistance of others increases. Informal caregivers, such as family members, friends, or neighbors, often provide this necessary assistance.

A study of 302 caregivers of people with MS determined that assistance was most often provided for mobility-related activities.[34] The stress and physical burden of caring for a friend or relative with MS may affect the health of caregivers and increase their own requirement for healthcare resources. Informal caregivers have been described as the 'hidden patient', due to the physical, emotional, psychologic, social, and economic burdens that are assumed in their role as caregiver.[35] In one survey on the level of MS caregiver strain, 12 % of caregivers reported receiving treatment for depression.[36] In another study, disease impact was found to be correlated with health problems in caregivers that affected both their physical and mental health status, including anxiety, depression, back pain, and insomnia.[37] Caregivers of people with MS experience a substantial burden and reductions in QoL, but this is less well recognized or studied than the effects on the patient.[38]

In addition to the stress and physical burden felt by the caregivers of people with MS, there is also an economic cost to their role. The adverse effect of MS on the patient's employment and the employment of others in the household invariably decreases the household's income and standard of living through reductions in salary or loss of future earnings.[12] The number of working days lost by caregivers is often similar to that lost by the MS patient. Kahn et al. found that 64.5 % of MS caregivers reported having to make work adjustments, such as taking time off.[36] An Italian study found that 39.3 % of caregivers lost an average 7.8 working days during a 3-month period,[39] and another found that female gender and advanced age were the main predictors of lower QoL in caregivers.[40] A more recent study in the US reported that 53 % of caregivers lost an average 7.3 work days in last year.[41]

Table 1: Tests Used for the Specific Assessment of Mobility, Ambulation, Walking, and Gait in Multiple Sclerosis

Test	Purpose	Details of Assessment Included	Equipment Needed, Time to Perform, and Cost	Validity of Data, Advantages/Disadvantages
Dynamic Gait Index (DGI)	Assess aspects of gait and balance during walking	Series of 8 tasks including walking at different speeds for fixed times, walking and keeping balance while head is turned or tilted, stepping over or around obstacles, and climbing stairs	Open area needed to conduct test; easy to conduct; 20–30 minutes; minimal cost	Reliable functional assessment tool; inversely correlated with timed walk; good concurrent validity;[47] poor discrimination between faller and nonfaller[85]
12-Item Multiple Sclerosis Walking Scale (MSWS-12)	Provide a patient-based measure of walking ability in MS	12 questions with responses rated on a scale of 1 (not at all) to 5 (extremely) about decreased ability to walk, run, or stand, walking difficulty, and support needed, etc.	Test forms, pen; interview with neurologist; easy to conduct; 15–20 minutes; minimal cost	More responsive than the FAMS-TOI mobility scale, the SF-36 Health Survey physical functioning scale, the EDSS, the Timed 25-Foot Walk test, and the GNDS[49]
Timed 25-Foot Walk (T25FW) test	Part of the MSFC	Patient is timed walking 25 feet as fast as possible without injury	Open area, stopwatch, pen; easy to conduct; low cost	High inter-rater and good concurrent validity;[86] does not distinguish gait changes resulting from fatigue;[87] predictor of long-term disability;[88] may provide poor estimate of maximum walking speed[89]
6-Minute Walk (6MW) test	Provide a measure of overall mobility and physical functioning	Distance walked is measured over a 6-minute time period; walking is self-paced	Open area, stopwatch, pen; easy to conduct; 6 minutes to complete plus time for recovery; minimal cost	Provides valuable information on effects of fatigue on ambulation; does not address qualitative changes or changes over the 6-minute period;[54] good test–retest reliability[53]
Timed Up and Go Test (TUGT)	Assess propensity for falling and general mobility in the elderly	Subjects are instructed to stand up, using chair armrests, walk to a line 3 m away, turn, and return to the chair	Armchair, stopwatch, tape measure; easy to conduct; 1–5 minutes to complete; minimal cost	Acceptable concurrent validity; poor discrimination between faller and nonfaller;[85] good test–retest reliability;[53] correlated with gait parameters, cognitive function, and behavior in people with MS[58]
Six Spot Step Test (SSST)	Quantitative measurement of ambulation in MS; a lower-limb counterpart to the 9HPT	Subjects are required to walk down a marked test field/floor and push wooden blocks out of circles in a specific order with the same foot each time	Marked test field, wooden blocks, stopwatch; 5–10 minutes to complete; low cost	Only moderately correlated with the EDSS and MSIS; superior to Timed 25-Foot Walk test for dynamic range, floor effect, and discriminatory power[57]
Hauser Ambulation Index (HAI)	Subjective assessment of walking ability and dependence on a wheelchair	Questions rate subjects on a scale of 1 (fully active) to 9 (wheelchair-bound and unable to transfer oneself independently); walking time is used together with other factors to rate the patients on an ordinal scale with 11 gradations	Stopwatch, test form, pen; 1–5 minutes to complete; minimal cost	Good inter-rater and test–retest reliability and convergent validity;[43] acceptable concurrent validity; poor discrimination between faller and nonfaller;[85] replaced by the T25FW in clinical studies due to more desirable psychometric properties
Kinetic and Kinematic Analysis (KKA)	Provide precise, objective data on gait during walking	Test determines force and angle of joints during gait cycle and provides data on spatial and temporal gait parameters	Requires special training and equipment; high cost of equipment	Biomechanics may not reflect activity limitations/participation restrictions; moderate reliability in pediatric population;[90] gait patterns varied according to severity of walking impairment in people with MS[59]
Functional Independence Measure (FIM)	Assess physical and cognitive disability focusing on the burden of care	Includes 18 items: 13 are physical domains based on the Barthel Index and 5 are cognition items; each item is scored from 1 to 7 (1 = total dependence and 7 = complete independence); score range from 18 to 126 (higher = greater ability)	Requires training; 15 minutes to complete; low cost	Acceptable inter-rater reliability and high internal validity;[44] similar responsiveness to the Barthel Index[46]
Rivermead Mobility Index (RMI)	Assess aspects of mobility	Patients are asked 15 yes/no questions regarding turning over in bed, lying to, sitting, sitting balance, standing, using, the stairs getting up off the floor, bathing, and running; maximum score = 15	Test forms, pen; 5–10 minutes to complete; minimal cost	Good reliability and internal validity[91,92]
Observation	Clinical observation of patient's gait and walking ability in a controlled setting	Patients are asked to walk while being observed by a neurologist	Requires training to recognize normal and abnormal gait characteristics; easy to conduct; 5–10 minutes to complete; minimal cost	Poor inter-rater reliability[93]

Table 1: Cont.

Test	Purpose	Details of Assessment Included	Equipment Needed, Time to Perform, and Cost	Validity of Data, Advantages/Disadvantages
Rivermead Visual Gait Assessment (RVGA)	Clinical observation of patient's gait and walking ability in a controlled setting	Patients are observed walking by a clinician trained in gait analysis, and scored on 20 observations, using a 4-point scale to indicate the degree of abnormality. Score ranges from 0 (normal gait) to 59 (abnormality)	Requires training to recognize normal and abnormal gait characteristics; time consuming to run	Good inter-rater and intra-rater reliability, displays sensitivity to treatment effects[48]

9HPT = 9-Hole Peg Test; EDSS = Expanded Disability Status Scale; FAMS-TOI = Family Assessment of Multiple Sclerosis Trial Outcome Index; GNDS = Guy's Neurological Disability Scale; MSIS = Multiple Sclerosis Impact Scale; MSFC = Multiple Sclerosis Functional Composite; SF = short-form. Adapted from Kesselring.[94]

Impaired Mobility Assessment Tools

There is increasing recognition of the importance of walking limitations in the lives of people with MS. Measuring mobility limitations in people with MS is essential to enable evaluation of disability and disease progression. Moreover, such measurements can provide valuable information on the efficacy of disease-modifying drugs, symptomatic agents, and rehabilitation strategies in people with MS. A variety of scales has been used for the measurement of mobility, ambulation, walking, and gait in MS. These include clinical rating scales, performance and physiologic markers, and alterations in spatial and temporal gait parameters. The EDSS is the gold standard for the measurement of MS disease severity, and although it is weighted toward ambulation at and above a score of 4.0, it is only marginally useful for measuring changes in mobility.[42] *Table 1* offers a summary of the mobility assessment tools used to characterize mobility impairment in people with MS. The Hauser Ambulation Index (HAI),[43] similar to the EDSS, has a high reliability and is effective in classifying patients based on their current walking ability; however, it demonstrates a low responsiveness to change, making it of limited use for measuring changes in mobility. Other clinical rating scales include the Functional Independence Measure (FIM) (an 18-item scale of physical and cognitive disability)[44] and the Barthel Index (a 10-component scale that measures ADL, widely used to assess disabilities caused by neurologic disease, especially stroke).[45] The FIM showed no superiority over the Barthel Index in people with MS undergoing neurorehabilitation,[46] and although the FIM is a reliable and valid tool, like the EDSS and AI, it exhibits low responsiveness to change.

The Dynamic Gain Index (DGI) relies on an observer's rating of the patient's limitations while performing specific tasks, and measures walking, stair climbing, and balance.[47] Although it has demonstrated good reliability and has been found to inversely correlate with timed walk tests, the major limitation of this assessment is that a trained evaluator must run the test. Similarly, the Rivermead Visual Gait Assessment (RVGA), while providing qualitative information on the walking ability of a patient, is time consuming, has complex scoring, and must be performed by a clinician with experience in gait analysis.[48]

The self-reported 12-item MS walking (MSWS-12) scale was specifically developed to measure walking ability in MS,[49] and has since been adapted into a generic measure of walking and mobility, renamed the Walk-12.[50] The MSWS-12 is a patient-rated measure of walking, and contains 12 questions with Likert-type responses. It has been demonstrated to be more responsive than the Timed 25-Foot Walk (T25FW) test,[49] and multiple studies have confirmed the validity of the MSWS-12 as a measure of the impact of MS on walking.[49,51,52]

Timed walk tests are objective, quantitative measures of walking, and many have the advantage of requiring minimum time and space.[42] In general, shorter timed walking tests, such as the T25FW, the 10 m timed walk (10MTW), and the 30 m timed walk (30MTW), assess the patient's overall walking disability. Longer-distance walking tests, such as the 6-minute walk (6MW), the 2-minute walk (2MW), and the 100 m timed walk (100MTW) are better at assessing fatigue during walking, and limitations in walking distance. The T25FW, which measures the time taken for the patient to walk 25 feet, has shown good reliability and reproducibility in multiple studies, has been extensively validated, and is often used as a standard for evaluating other walking and mobility assessments.[53] The 6MW measures the maximum distance that a patient can walk in 6 minutes, is reproducible,[54] and has been shown to correlate well with other disability measures.[53] The 6MW requires more space than other timed walked tests and is more a measure of walking endurance than walking speed. An alternative to the 6MW is the 2MW test (measuring the maximum distance that a patient can walk in 2 minutes), which has reduced patient burden, especially for those with high levels of fatigue.[55]

Other timed mobility tests include the Timed Up and Go Test (TUGT),[56] and Six Spot Step Test (SSST).[57] The TUGT is easy to administer and measures the time taken for a patient to rise from a chair, walk 3 m, turn around, walk back to the chair, and sit down. The TUGT has been demonstrated to correlate with motor, cognitive, and behavioral functioning in relapsing-remitting MS.[58] The SSST measures lower-extremity function more than the other walking tests, and also measures coordination and balance.[57] In this test, the patient is asked to walk between cylindrical blocks placed on the floor in a set pattern; each cylinder is stood in marked circle. As the patient walks, he or she is required to kick the block out of each circle with a specified foot until all the cylinders have been knocked over. Patients repeat the process four times (twice using each foot).

While timed tests can measure changes in walking speed, they are unable to measure differences in gait pattern. The RVGA assesses gait pattern but, as mentioned previously, requires a clinician with experience in gait analysis. A recent study assessed the biomechanical characteristics of gait among people with MS with varying degrees of severity using kinetic and kinematic analysis (KKA)[59] and there is increasing interest in these types of measures for assessing mobility in people with MS. Motion

analysis systems can provide a 3D assessment of gait kinetics and kinematics; however, they require large amounts of space, analysis is time consuming, and the equipment needed has a high cost.[42] The GAITrite® (Sparta NJ, US) electronic pathway appears to be a promising tool for gait analysis has been demonstrated to identify mobility impairment in people with MS with a relatively short disease duration.[60] Recently, accelerometry has been recognized as a tool for the assessment of real-life walking ability in people with MS,[61] and similarly pedometry can also be used outside of the clinic to measure changes in patient mobility.

In summary, there are many measurement tools for mobility impairment in MS; however, they have varying degrees of responsiveness to change, ease of use, and cost. The T25FW and the MSWS-12 are both feasible for use in clinical practice, while also displaying satisfactory reliability and responsiveness.[42] The T25FW is the best characterized measure of mobility in people with MS, and it was recently proposed that the T25FW and the 2MW test be used as standards for measuring walking capacity in MS.[62]

Therapeutic Options for Treating Mobility in Multiple Sclerosis

One therapeutic option for treating mobility in people with MS is exercise and physical therapy. People with MS often have decreased physical activity, leading to physical deconditioning, which may in turn influence the start and progression of mobility impairment (see *Figure 1*).[63–65] Decreased physical activity leads to reduced aerobic capacity, balance, and muscle strength, which feeds back to further reduce physical activity (stage 1 of *Figure 1*).[63] At some point in this feedback loop a threshold is met, resulting in an impact on the patient's mobility (stage 2 of *Figure 1*). Evidence from several studies indicates that exercise and physical therapy may have a beneficial effect on mobility, while also improving fitness, muscle strength, fatigue, mood, and QoL.[63,65–69] A meta-analysis examining the overall effect of exercise on QoL in people with MS, found that exercise training is associated with a small but statistically significant improvement in QoL.[66] Furthermore, a Cochrane systematic review concluded that exercise therapy can be beneficial for people with MS in terms of isometric strength, physical fitness, and mobility-related ADL.[67] A recent pilot study examined changes in walking function in people with MS following aerobic, resistance, and balance-related exercise training, and improved walking mobility following exercise training was demonstrated, as determined by improvements in MSWS-12 score, T26FW, and TUGT.[70] Further research is needed to fully determine the effects of exercise on mobility in people with MS. Although this field of study is not sufficiently developed, the preliminary evidence is promising.

Impaired walking in MS can be considered a disease-specific disability resulting from the conduction blockade that is a consequence of axonal demyelination. While current immunomodulatory therapies for MS slow disease progression and reduce relapse rates in clinically isolated syndrome and remitting forms of MS,[71–73] immunomodulatory treatments do not necessarily provide any improvement in mobility. Approximately 50 % of people with MS report no improvement in mobility following DMT.[13,74] Current medications that target mobility impairment in people with MS include US Food and Drug Administration (FDA)-approved dalfampridine extended-release (dalfampridine-ER) tablets, known as sustained-, prolonged-, or modified-release fampridine outside the US.

Table 2: Mobility Assistive Technologies for People with Multiple Sclerosis

MAT	Use
AFOs	Used to control foot drop, and unstable knee and ankle musculature
FES	Used for foot drop, balance, and walking training during rehabilitation treatment
HFAOs	Used for people with MS who do not effectively ambulate despite the use of an AFO or FES
Canes	Beneficial when walking is only mildly unstable, to reduce walking effort and risk of falls
Crutches	Helpful for balance, widening the base of support, and decreasing weight bearing
Walkers and/or wheeled walkers (rollators)	Used by people with moderate deficits to provide increased stability. A walker provides a larger footprint compared with cane or crutches
Manual wheelchairs	A stable wheeled device that still provides some level of a physical activity
PAPAWs	PAPAWs are manual wheelchairs with a force/moment-sensing pushrim, which provides assistance with wheelchair propulsion. Requires less physical strain than a manual chair, useful for patients with fatigue
Scooters	Motorized mobility aid for moderate to advanced MS. The lack of stability during turns and limited seating system options can be problematic
Power wheelchairs	Used as mobility option for advanced stages but also recommended as a MAT option for patients with fatigue

AFO = ankle–foot orthoses; FES = functional electrical stimulation; HFAO = hip flexion assist orthoses; MAT = mobility assistive technologies; MS = multiple sclerosis; PAPAWs = power-assisted pushrim-activated wheelchairs.

Dalfampridine is not an immunomodulatory treatment, but it can be used in combination with DMTs, and specifically targets walking impairment.

Dalfampridine, a broad-spectrum inhibitor of potassium channels, is believed to exert its effects by binding to potassium channels in the cellular membranes of CNS nerve fibers, particularly in the areas of demyelination.[75] The blockade of potassium channels has been shown to increase conduction in demyelinated nerve fibers.[76] Dalfampridine improves action potential propagation by binding to the open potassium channel transmembrane pore region, which delays repolarization of the nerve cell, and in turn increases the duration of the action potential.[10,76]

Dalfampridine-ER has been demonstrated to improve walking in people with MS.[77,78] Two phase III trials assessing the effects of dalfampridine on walking in people with MS demonstrated that dalfampridine has a positive effect on walking speed.[79,80] In both studies, the primary outcome was percentage of T25FW responders, defined as patients who had a consistent improvement in T25FW speed relative to baseline. A 2009 phase III randomized trial of dalfampridine-ER 10 mg twice daily compared with placebo, found that 35 % of patients in the intent-to-treat (ITT) population (n=224) were responders to dalfampridine-ER, whereas 8% of patients taking placebo demonstrated T25FW improvement.[80] Additionally, walking speed in dalfampridine responders increased by 25.2 % from baseline, and leg strength (as measured by the lower extremity manual muscle test [LEMMT]) was also significantly increased in this group compared with placebo (0.18 versus 0.04 [p=0.0002]). In a second randomized double-blind phase III trial, 42.9 % responded

to dalfampridine compared with 9.3 % of those in the placebo group. The average improvement in walking speed in the dalfampridine-responder group was 24.7 % from baseline.[79] Dalfampridine is generally well tolerated and most adverse events are mild.[77,81]

Mobility-related Assistive Technology

When mobility deficits do not respond to other interventions, mobility-related assistive technology (MAT) may be helpful. Despite best treatment efforts, assistance with walking will eventually be required by 75–80 % of all people with MS (with relapsing-remitting or primary progressive MS).[31] The use of MAT can greatly improve ADL and the independence of people with MS.[82] Common MATs used by people with MS are summarized in *Table 2*.

A survey of 703 self-reporting working-age adults with MS reported significant mobility problems, including an increased level of concentration required to walk and difficulty in standing.[19] The same survey indicated that 60.5 % of patients required a mobility aid, with manual wheelchairs the most common,[19] and that patients often alternated between mobility aids to suit their specific mobility requirements. Several studies have found that manual wheelchairs are the most common MATs utilized by people with MS.[9,83,84]

Caution should be used when prescribing MATs because if the device does not fit the patient's needs it is often abandoned. A retrospective study found that MAT devices were abandoned in people with MS for several main reasons: worsening in physical status (36.4 %), nonacceptance by the user (30.3 %), inappropriateness (24.2 %), and insufficient/lack of information and training given to the patient (9.0 %).[83] To be adopted successfully, the MAT must increase QoL in people with MS.[6] The challenge for rehabilitation specialists is to find an appropriate device that meets the user's needs, such as level of fatigue, degree of mobility impairment, and the activities they wish to participate in. Successful adoption of MAT devices involves a high level of communication between the patient, the rehabilitation team, family members, and caregivers.

Experiences with Mobility from a Multiple Sclerosis Nurse Practitioner and a Neurologist

The Stanford Multiple Sclerosis Center sees approximately 800 people with MS each year. It is a specialty clinic within the larger neurosciences clinic and therefore often sees patients for second and third opinions on diagnosis and treatment of MS. Of this population seen each year, more than 75 % complain of some difficulty with walking. Among patients in this population who have difficulty with walking, more than 90 % have resorted to using a walking aid. The walking aid serves the purpose of maintaining safety through assistance, but is inadequate in serving the patient's need for independence and efficacy. The center proactively treats the disease course with DMTs to hopefully reduce relapses and further delay disease progression. But, as has been seen, patients will continue to progress in disability over time.

In combination with DMTs, the Stanford Multiple Sclerosis Center team looks for patient-specific complementary approaches to treat the symptoms of MS. Patients with a walking impairment also struggle with symptoms that can worsen their gait. Fatigue is one of the most common symptoms and, combined with walking impairment, is a significant disabling feature in the patient population. The Stanford Multiple Sclerosis Center providers consider various agents to address fatigue including antidepressants, stimulants, and other complementary therapies. In addition, the importance of body conditioning, exercise, stretching, and stress reduction is emphasized to help with symptoms. Dalfampridine-ER is frequently prescribed to help with walking impairment and the patient response has paralleled that observed in clinical trials. In anecdotal reports, those patients who benefit from dalfampridine-ER have remarked that their QoL has substantially improved with its use, which they were unable to perceive with the use of walking aids.

A patient's perception of wellness is complicated by not only their neurologic status, but also by their physical appearance and emotional tolerance to their disability. In general, patients appear to have a harder time accepting the use of a walking aid rather than a medication that can potentially help their walking outcome. Given this, the patient's perceived sense of wellness is improved by reduced dependence on walking aids. Nevertheless, the nature of this disorder will evolve into disability progression. Addressing the concerns of walking impairment and MS symptoms early has helped provide better patient outcomes in the long-term management of MS. In the future, the Stanford Multiple Sclerosis Center team hopes to see additional treatments and mobility assistance become available to help patients function and live independently.

Conclusions

Loss of mobility is among the most disabling effects of MS, and it adversely affects independence, employment, and QoL. As mobility decreases, informal caregivers such as family members, friends, and neighbors provide an important role in assisting with mobility-related activities. Physical, emotional, psychologic, social, and economic burdens, however, are often a consequence of their caregiving role. Measuring mobility limitations in people with MS is essential to enable evaluation of disability and disease progression, and can provide valuable information on the efficacy of disease-modifying drugs, symptomatic agents, and rehabilitation strategies in people with MS. Current treatments that target walking impairment in MS include dalfampridine-ER which has been demonstrated in clinical trials and in regular clinical use to have beneficial effects on walking in people with MS. Other approaches involve physical therapy and exercise. If walking impairments do not respond to therapeutic interventions, MAT may be helpful. To be adopted successfully, the MAT must increase the QoL in people with MS, and must involve a high level of communication between the patient, the rehabilitation team and family members and caregivers. ■

1. Bjartmar C, Trapp BD, Axonal and neuronal degeneration in multiple sclerosis: mechanisms and functional consequences, *Curr Opin Neurol,* 2001;14:271–8.
2. WHO, World Health Organization: Multiple Sclerosis International Federation. Atlas: Multiple Sclerosis Resources in the World 2008. Geneva, Switzerland: World Health Organization; 2008. Available at: http://www.who.int/mental_health/neurology/en (accessed November 3, 2012).
3. National Multiple Sclerosis Society, *Multiple Sclerosis Information Sourcebook*, New York, NY: Information Resource Center and Libraryof the National Multiple Sclerosis Society, 2005.
4. Martin CL, Phillips BA, Kilpatrick TJ, et al., Gait and balance impairment in early multiple sclerosis in the absence of clinical disability, *Mult Scler,* 2006;12:620–28.
5. Polman CH, Reingold SC, Edan G, et al., Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria", *Ann Neurol,* 2005;58:840–46.
6. Souza A, Kelleher A, Cooper R, et al., Multiple sclerosis and mobility-related assistive technology: systematic review of literature, *J Rehabil Res Dev*, 2010;47:213–23.
7. Pike J, Jones E, Rajagopalan K, et al., Social and economic burden of walking and mobility problems in multiple sclerosis, *BMC Neurol*, 2012;12:94.
8. Sutliff MH, Contribution of impaired mobility to patient burden in multiple sclerosis, *Curr Med Res Opin,* 2010;26:109–19.
9. Baum HM, Rothschild BB, Multiple sclerosis and mobility restriction, *Arch Phys Med Rehabil*, 1983;64:591–6.
10. Bever CT, Judge SI, Sustained-release fampridine for multiple sclerosis, *Expert Opin Investig Drugs,* 2009;18:1013–24.
11. Heesen C, Bohm J, Reich C, et al., Patient perception of bodily

functions in multiple sclerosis: gait and visual function are the most valuable, *Mult Scler,* 2008;14:988–91.
12. Dunn J, Impact of mobility impairment on the burden of caregiving in individuals with multiple sclerosis, *Expert Rev Pharmacoecon Outcomes Res*, 2010;10:433–40.
13. Hemmett L, Holmes J, Barnes M, et al., What drives quality of life in multiple sclerosis?, *QJM*, 2004;97:671–6.
14. Wu N, Minden SL, Hoaglin DC, et al., Quality of life in people with multiple sclerosis: data from the Sonya Slifka Longitudinal Multiple Sclerosis Study, *J Health Hum Serv Adm,* 2007;30:233–67.
15. Jones CA, Pohar SL, Warren S, et al., The burden of multiple sclerosis: a community health survey, *Health Qual Life Outcomes,* 2008;6:1.
16. Motl RW, Snook EM, Schapiro RT, Symptoms and physical activity behavior in individuals with multiple sclerosis, *Res Nurs Health*, 2008;31:466–75.
17. Finlayson M, van Denend T, Experiencing the loss of mobility: perspectives of older adults with MS, *Disabil Rehabil*, 2003;25:1168–80.
18. Peterson EW, Cho CC, Finlayson ML, Fear of falling and associated activity curtailment among middle aged and older adults with multiple sclerosis, *Mult Scler,* 2007;13:1168–75.
19. Iezzoni LI, Rao SR, Kinkel RP, Patterns of mobility aid use among working-age persons with multiple sclerosis living in the community in the United States, *Disabil Health J,* 2009;2:67–76.
20. Myhr KM, Riise T, Vedeler C, et al., Disability and prognosis in multiple sclerosis: demographic and clinical variables important for the ability to walk and awarding of disability pension, *Mult Scler,* 2001;7:59–65.
21. Poser CM, Brinar VV, Diagnostic criteria for multiple sclerosis, *Clin Neurol Neurosurg*, 2001;103:1–11.
22. Polman CH, Reingold SC, Banwell B, et al., Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria, *Ann Neurol,* 2011;69:292–302.
23. Iezzoni LI, Rao SR, Kinkel RP, Experiences acquiring and using mobility aids among working-age persons with multiple sclerosis living in communities in the United States, *Am J Phys Med Rehabil*, 2010;89:1010–23.
24. Trisolini M, Honeycutt A, Wiener J, Lesesne S, *Multiple Sclerosis International Federation Global Economic Impact of Multiple Sclerosis*, London: Multiple Sclerosis International Federation, 2010.
25. Chandraratna D, *MSIF survey on Employment and MS*, London: Multiple Sclerosis International Federation, 2010.
26. Salter AR, Cutter GR, Tyry T, et al., Impact of loss of mobility on instrumental activities of daily living and socioeconomic status in patients with MS, *Curr Med Res Opin*, 2010;26:493–500.
27. Larocca NG, Impact of walking impairment in multiple sclerosis: perspectives of patients and care partners, *Patient*, 2011;4:189–201.
28. Kurtzke JF, Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS), *Neurology*, 1983;33:1444–52.
29. Nortvedt MW, Riise T, Myhr KM, et al., Quality of life in multiple sclerosis: measuring the disease effects more broadly, *Neurology*, 1999;53:1098–103.
30. Confavreux C, Vukusic S, Adeleine P, Early clinical predictors and progression of irreversible disability in multiple sclerosis: an amnesic process, *Brain*, 2003;126:770–82.
31. Confavreux C, Vukusic S, Moreau T, et al., Relapses and progression of disability in multiple sclerosis, *N Engl J Med,* 2000;343:1430–38.
32. Kobelt G, Berg J, Lindgren P, et al., Costs and quality of life of patients with multiple sclerosis in Europe, *J Neurol Neurosurg Psychiatry*, 2006;77:918–26.
33. Edgley K, Sullivan MJ, Dehoux E, A survey of multiple sclerosis, part II: determinants of employment status, *Can J Rehabil*, 1991;4:127–32.
34. Finlayson M, Cho C, A descriptive profile of caregivers of older adults with MS and the assistance they provide, *Disabil Rehabil*, 2008;30:1848–57.
35. Buhse M, Assessment of caregiver burden in families of persons with multiple sclerosis, *J Neurosci Nurs,* 2008;40:25–31.
36. Khan F, Pallant J, Brand C, Caregiver strain and factors associated with caregiver self-efficacy and quality of life in a community cohort with multiple sclerosis, *Disabil Rehabil*, 2007;29:1241–50.
37. Forbes A, While A, Mathes L, Informal carer activities, carer burden and health status in multiple sclerosis, *Clin Rehabil*, 2007;21:563–75.
38. Opara J, Jaracz K, Brola W, Burden and quality of life in caregivers of persons with multiple sclerosis, *Neurol Neurochir Pol*, 2012;46:472–9.
39. Amato MP, Battaglia MA, Caputo D, et al., The costs of multiple sclerosis: a cross-sectional, multicenter cost-of-illness study in Italy, *J Neurol*, 2002;249:152–63.
40. Patti F, Amato MP, Battaglia MA, et al., Caregiver quality of life in multiple sclerosis: a multicentre Italian study, *Mult Scler*, 2007;13:412–19.
41. Quig MS, Simsarian J, Cutter G, et al., MS CarePartner Stress: a NARCOMS study, *Multiple Sclerosis Quarterly Report,* 2007;29:6–10.
42. Bethoux F, bennett S, Evaluating walking in patients with multiple sclerosis: which assessment tooks are useful in clinical practice?, *Int J MS Care,* 2011;13:4–14.
43. Hauser SL, Dawson DM, Lehrich JR, et al., Intensive immunosuppression in progressive multiple sclerosis. A randomized, three-arm study of high-dose intravenous cyclophosphamide, plasma exchange, and ACTH, *N Engl J Med*, 1983;308:173–80.
44. Ottenbacher KJ, Hsu Y, Granger CV, et al., The reliability of the functional independence measure: a quantitative review, *Arch Phys Med Rehabil*, 1996;77:1226–32.
45. Quinn TJ, Langhorne P, Stott DJ, Barthel index for stroke trials: development, properties, and application, *Stroke*, 2011;42:1146–51.
46. van der Putten JJ, Hobart JC, Freeman JA, et al., Measuring change in disability after inpatient rehabilitation: comparison of the responsiveness of the Barthel index and the Functional Independence Measure, *J Neurol Neurosurg Psychiatry*, 1999;66:480–84.
47. McConvey J, Bennett SE, Reliability of the Dynamic Gait Index in individuals with multiple sclerosis, *Arch Phys Med Rehabil,* 2005;86:130–33.
48. Lord SE, Halligan PW, Wade DT, Visual gait analysis: the development of a clinical assessment and scale, *Clin Rehabil*, 1998;12:107–19.
49. Hobart JC, Riazi A, Lamping DL, et al., Measuring the impact of MS on walking ability: the 12-Item MS Walking Scale (MSWS-12), *Neurology*, 2003;60:31–6.
50. Holland A, O'Connor RJ, Thompson AJ, et al., Talking the talk on walking the walk: a 12-item generic walking scale suitable for neurological conditions?, *J Neurol*, 2006;253:1594–602.
51. Motl RW, Snook EM, Confirmation and extension of the validity of the Multiple Sclerosis Walking Scale-12 (MSWS-12), *J Neurol Sci*, 2008;268:69–73.
52. McGuigan C, Hutchinson M, Confirming the validity and responsiveness of the Multiple Sclerosis Walking Scale-12 (MSWS-12), *Neurology*, 2004;62:2103–5.
53. Learmonth YC, Paul L, McFadyen AK, et al., Reliability and clinical significance of mobility and balance assessments in multiple sclerosis, *Int J Rehabil Res,* 2012;35:69–74.
54. Goldman MD, Marrie RA, Cohen JA, Evaluation of the six-minute walk in multiple sclerosis subjects and healthy controls, *Mult Scler*, 2008;14:383–90.
55. Butland RJ, Pang J, Gross ER, et al., Two-, six-, and 12-minute walking tests in respiratory disease, *Br Med J (Clin Res Ed)*, 1982;284:1607–8.
56. Podsiadlo D, Richardson S, The timed "Up & Go": a test of basic functional mobility for frail elderly persons, *J Am Geriatr Soc*, 1991;39:142–8.
57. Nieuwenhuis MM, Van Tongeren H, Sorensen PS, et al., The six spot step test: a new measurement for walking ability in multiple sclerosis, *Mult Scler,* 2006;12:495–500.
58. Allali G, Laidet M, Assal F, et al., Adapted Timed Up and Go: A Rapid Clinical Test to Assess Gait and Cognition in Multiple Sclerosis, *Eur Neurol,* 2012;67:116–20.
59. Kelleher KJ, Spence W, Solomonidis S, et al., The characterisation of gait patterns of people with multiple sclerosis, *Disabil Rehabil*, 2010;32:1242–50.
60. Givon U, Zeilig G, Achiron A, Gait analysis in multiple sclerosis: characterization of temporal-spatial parameters using GAITRite functional ambulation system, *Gait Posture*, 2009;29:138–42.
61. Weikert M, Suh Y, Lane A, et al., Accelerometry is associated with walking mobility, not physical activity, in persons with multiple sclerosis, *Med Eng Phys*, 2012;34(5):590–97.
62. Gijbels D, Dalgas U, Romberg A, et al., Which walking capacity tests to use in multiple sclerosis? A multicentre study providing the basis for a core set, *Mult Scler*, 2012;18:364–71.
63. Motl RW, Goldman MD, Benedict RH, Walking impairment in patients with multiple sclerosis: exercise training as a treatment option, *Neuropsychiatr Dis Treat*, 2010;6:767–74.
64. Weikert M, Motl RW, Suh Y, et al., Accelerometry in persons with multiple sclerosis: measurement of physical activity or walking mobility?, *J Neurol Sci,* 2010;290:6–11.
65. White LJ, Castellano V, Exercise and brain health – implications for multiple sclerosis. Part 1 – neuronal growth factors, *Sports Med*, 2008;38:91–100.
66. Motl RW, Gosney JL, Effect of exercise training on quality of life in multiple sclerosis: a meta-analysis, *Mult Scler*, 2008;14:129–35.
67. Rietberg MB, Brooks D, Uitdehaag BM, et al., Exercise therapy for multiple sclerosis, *Cochrane Database Syst Rev,* 2005;CD003980.
68. Andreasen AK, Stenager E, Dalgas U, The effect of exercise therapy on fatigue in multiple sclerosis, *Mult Scler,* 2011;17:1041–54.
69. Snook EM, Motl RW, Effect of exercise training on walking mobility in multiple sclerosis: a meta-analysis, *Neurorehabil Neural Repair*, 2009;23:108–16.
70. Motl RW, Smith DC, Elliott J, et al., Combined training improves walking mobility in persons with significant disability from multiple sclerosis: a pilot study, *J Neurol Phys Ther,* 2012;36:32–7.
71. Freedman MS, Hughes B, Mikol DD, et al., Efficacy of disease-modifying therapies in relapsing remitting multiple sclerosis: a systematic comparison, *Eur Neurol*, 2008;60:1–11.
72. Rovaris M, Confavreux C, Furlan R, et al., Secondary progressive multiple sclerosis: current knowledge and future challenges, *Lancet Neurol*, 2006;5:343–54.
73. Miller DH, Leary SM, Primary-progressive multiple sclerosis, *Lancet Neurol*, 2007;6:903–12.
74. Zwibel HL, Contribution of impaired mobility and general symptoms to the burden of multiple sclerosis, *Adv Ther*, 2009;26:1043–57.
75. Espejo C, Montalban X, Dalfampridine in multiple sclerosis: from symptomatic treatment to immunomodulation, *Clin Immunol*, 2012;142:84–92.
76. Judge SI, Bever CT, Jr., Potassium channel blockers in multiple sclerosis: neuronal Kv channels and effects of symptomatic treatment, *Pharmacol Ther,* 2006;111:224–59.
77. Hayes KC, Impact of extended-release dalfampridine on walking ability in patients with multiple sclerosis, *Neuropsychiatr Dis Treat*, 2011;7:229–39.
78. Goodman AD, Brown TR, Cohen JA, et al., Dose comparison trial of sustained-release fampridine in multiple sclerosis, *Neurology*, 2008;71:1134–41.
79. Goodman AD, Brown TR, Edwards KR, et al., A phase 3 trial of extended release oral dalfampridine in multiple sclerosis, *Ann Neurol*, 2010;68:494–502.
80. Goodman AD, Brown TR, Krupp LB, et al., Sustained-release oral fampridine in multiple sclerosis: a randomised, double-blind, controlled trial, *Lancet*, 2009;373:732–8.
81. Jara M, Barker G, Henney HR, 3rd, Dalfampridine extended release tablets: 1 year of postmarketing safety experience in the US, *Neuropsychiatr Dis Treat*, 2013;9:365–70.
82. Ambrosio F, Boninger ML, Fitzgerald SG, et al., Mobility device as a determinant of social participation in persons with multiple sclerosis, Proceedings of the RESNA, 26th Annual Conference, Atlanta, Georgia, 2003.
83. Verza R, Carvalho ML, Battaglia MA, et al., An interdisciplinary approach to evaluating the need for assistive technology reduces equipment abandonment, *Mult Scler*, 2006;12:88–93.
84. Finlayson M, Guglielmello L, Liefer K, Describing and predicting the possession of assistive devices among persons with multiple sclerosis, *Am J Occup Ther*, 2001;55:545–51.
85. Cattaneo D, Regola A, Meotti M, Validity of six balance disorders scales in persons with multiple sclerosis, *Disabil Rehabil*, 2006;28:789–95.
86. Rudick RA, Cutter G, Reingold S, The multiple sclerosis functional composite: a new clinical outcome measure for multiple sderosis trials, *Mult Scler*, 2002;8:359–65.
87. Kaufman M, Moyer D, Norton J, The significant change for the Timed 25-foot Walk in the multiple sclerosis functional composite, *Mult Scler*, 2000;6:286–90.
88. Bosma LV, Kragt JJ, Knol DL, et al., Clinical scales in progressive MS: predicting long-term disability, *Mult Scler,* 2012;18:345–50.
89. Phan-Ba R, Pace A, Calay P, et al., Comparison of the timed 25-foot and the 100-meter walk as performance measures in multiple sclerosis, *Neurorehabil Neural Repair*, 2011;25:672–9.
90. Krebs DE, Edelstein JE, Fishman S, Reliability of observational kinematic gait analysis, *Phys Ther,* 1985;65:1027–33.
91. Hobart JC, Cano S, Improving the evaluation of therapeutic interventions in multiple sclerosis: the role of new psychometric methods, *Health Technol Assess*, 2009;13:ix-x, 1–177.
92. Collen FW, Wade DT, Robb GF, et al., The Rivermead mobility index: a further development of the rivermead motor assessment, *Int Disabil Stud,* 1991;13:50–54.
93. Hutchinson B, Forwell SJ, Bennett SE, et al., Towards a consensus on rehabilitation outcomes in MS: Gait and fatigue. Report of a CMSC consensus conference, *Int J MS Care,* 2009;11:12.
94. Kesselring J, Disease progression in multiple sclerosis II. Methods for the determination of walking impairment and its impact on activities and social participation, *European Neurological Review,* 2010;5(1):61–8.