

Veterans Health Administration Multiple Sclerosis Centers of Excellence: Clinical care, education, informatics, and research

In January 2002, the Department of Veterans Affairs (VA) established two Multiple Sclerosis (MS) Centers of Excellence (MSCoEs) to improve the care of veterans with MS. Since then, MSCoE East, based at the Baltimore VA Medical Center (VAMC), and MSCoE West, based at the Seattle and Portland VAMCs, have initiated a variety of clinical care, educational, and research initiatives (see www.va.gov/ms for more information). The MSCoEs are pleased to present this special issue of the *Journal of Rehabilitation Research and Development (JRRD)* devoted to MS.



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MS is an important neurologic disease among veterans. Up to 24,000 veterans with MS receive care through the Veterans Health Administration (VHA) and over 6,000 are service-connected for MS [1]. The total cost to the VHA for providing care and disability benefits to veterans with MS is considerable. A 1993 study reported average costs, including VA benefits and home healthcare, of \$35,000 per patient each year [2]. Importantly, cost of care rose significantly with increasing disability. With the advent of disease-modifying agents (DMAs) for MS, we expect that early treatment will decrease the disability associated with the disease and thereby enhance the health and health-related quality of life (QOL) of veterans with MS. Focusing on the healthcare needs of veterans with MS is important because veterans with MS differ significantly from nonveterans with MS. Compared with nonveterans, veterans with MS are more likely to be male and older and have a higher disability burden and progressive form of MS [3]. Research studies of nonveteran populations may not reflect the differing needs of veterans with MS.

This special issue of *JRRD* contains articles that (1) address an array of issues relevant to the care of veterans with MS and (2) reflect some of the initiatives being promoted by the two MSCoEs. Both MSCoEs embrace the chronic-care model first described by Wagner et al. [4–5]. Hatzakis et al. discuss implementation of a chronic-care model in MS

through use of a data repository, state-of-the-art informatics, existing clinical-care guidelines, educated providers and veterans, and continuous quality improvement through a network of facilities. The authors describe the key elements of an informatics infrastructure in support of an MS chronic-care model, including a VA National MS Data Repository that the MSCoEs have jointly built to serve clinical, research, and administrative goals. Culpepper et al. report on the early challenges in identifying veterans with MS based on existing electronic data sources. They verified, using electronic medical record review, that an algorithmic approach

can be used to identify a cohort that most likely has MS. Ensuring that healthcare providers are adequately educated about how to care for veterans with MS is also central to the chronic-care model. Turner and associates describe an educational needs assessment of VA and non-VA providers with a special interest in MS. This survey indicates that VA providers have similar self-identified educational needs as their community-based colleagues. Areas of particular need included education on management of cognitive impairment, fatigue, depression, spasticity, sexual dysfunction, and use of DMAs and development of an approach to the diagnosis of MS. This survey will provide the basis for the development of education programs by the MSCoEs that target VA MS healthcare providers.

Treatment of MS in the VA is challenging. Guarnaccia and colleagues report on their assessment of 204 veterans with MS undergoing treatment with a DMA at multiple VAMCs. This study documents that veterans starting DMAs differ significantly demographically from those participating in the initial clinical trials of these agents. For instance, compared with those in the pivotal trial that led to Food and Drug Administration approval for interferon β -1b, veterans starting DMAs were much more likely to be male, older by a mean of 6 years, more disabled as measured by the Expanded Disability Status Scale, and non-Caucasian (21% vs 7%). The differences in sex and race are striking and potentially of great importance, since they can affect responses to a variety of treatments. The results of MS treatment trials with predominantly female subjects and a low percentage of non-Caucasians may not generalize to veterans with MS. VAMC participation in multicenter clinical trials or separate trials conducted within the VHA should be encouraged so that DMAs are tested in populations that represent those receiving care for MS through the VHA.

Several articles in this issue address the important areas of cognitive impairment, depression, and fatigue, all of which are common and frequently disabling complications of MS and areas that providers have identified as priorities for research and education. Wallin and colleagues provide an excellent review of cognitive dysfunction in MS. Cognitive

impairment affects about 50 percent of people with MS, does not correlate well with physical impairment, has a significant impact on social functioning, is often under-recognized, and is difficult to assess and treat. The development of more accessible assessment tools should aid in recognizing this complication of MS and is a goal of the team at MSCoE East. Wallin et al. review another important complication of MS—depression. The lifetime risk of depression among people with MS is 40 to 60 percent. While this is a treatable complication of MS, it also is often under-recognized, can have a highly negative impact on QOL, and increases the risk of suicide. The authors present a useful paradigm for approaching the assessment of depression among patients with MS and a summary of treatments.

Lovera and associates present an interesting study looking at how well self-perception of cognitive dysfunction among people with MS predicts changes in objective measures of cognitive impairment. The Perceived Deficits Questionnaire (PDQ), part of the MS QOL Inventory, provides a self-assessment of perceived cognitive deficits. Among MS subjects participating in a clinical trial, these authors found that the PDQ did not correlate with two objective tests of cognitive dysfunction that are commonly abnormal in MS—the Paced Auditory Serial Addition Test and the California Verbal Learning Test. However, the PDQ did correlate with depression as assessed by the Beck Depression Inventory. The implications of this study are important. Individuals with MS who are reporting cognitive difficulties may well be depressed, and depression is easier to treat than cognitive impairment caused by MS.

Oken et al. present an analysis that provides a cautionary note for clinicians. They assessed the use of medications with potential central nervous system (CNS) side effects in participants with MS in a clinical trial. They found that subjects with MS taking one or more agents with CNS side effects had increased fatigue and were more impaired on measures of processing speed and sustained attention. While the study did not establish a causal association between medication use and effects on fatigue and these two measures of cognition, it clearly points to the need to include medication use

as a covariate in studies on fatigue and cognitive impairment. From a clinical perspective, the study also reinforces the importance of considering the potential CNS side effects of any medication prescribed to treat MS.

The article by Lewis et al. provides new insights into a common complaint among people with MS. Many individuals with MS complain of difficulty “hearing” in a noisy environment and this often interferes with their social interactions and can have a negative impact on employment. Despite these hearing complaints, people with MS usually have normal or near-normal pure tone audiometrical-test results. Lewis and colleagues have devised a method of quantitating speech perception in a noisy environment. They found that participants with MS had significantly impaired speech perception in a noisy environment compared with controls, despite relatively normal pure tone audiological-test results. This research group thus has created a way to measure abnormalities of speech perception in a noisy environment that should prove useful in assessing people with MS and unexplained hearing problems. In addition, frequency-modulation technology might prove useful in aiding hearing in people with MS who have significant speech discrimination difficulties in a noisy environment.

Several surveys have documented that complementary and alternative medicine (CAM) therapies are commonly used by people with MS. These therapies are often used to manage MS symptoms and improve QOL. Campbell et al. conducted a survey of veterans with MS and found that 37 percent of respondents reported current or past use of CAM. This is a lower percentage than has been reported in surveys of the general MS population. This may be because CAM use is often associated with female sex and higher income levels and the veteran population is predominantly male and has a lower income level than nonveteran populations. However, 37 percent is still substantial, and CAM use among veterans with MS warrants further investigation.

Judge et al. review new and old data regarding voltage-gated potassium channels as they relate to MS. Blockade of potassium channels with chemicals

such as 4-aminopyridine has been investigated for a number of years for the symptomatic treatment of MS. Potassium-channel blockade can improve conduction along chronically demyelinated axons, and clinical trials have suggested that 4-aminopyridine can improve motor fatigability. This continues to be an active area of clinical research, and a multicenter trial of 4-aminopyridine is currently under way. Newer data indicate that immune cells express voltage-gated potassium channels, and the authors hypothesize that potassium-channel blockade may be capable of immunomodulation in MS. The authors present a compelling case for investigating potassium channels as new therapeutic targets in MS.

Finally, Cudrici et al. review interesting data that suggest a dual role for complement activation in determining the fate of oligodendrocytes in experimental autoimmune encephalomyelitis (EAE) and, potentially, MS. Oligodendrocyte apoptosis occurs in both EAE and MS. Activation of the terminal complex C5b-9 in the complement cascade can promote demyelination and oligodendrocyte death. However, sublytic C5b-9 can protect oligodendrocytes from apoptosis. Thus, the complement system may have a Janus role in EAE and, by implication, MS, either killing or protecting oligodendrocytes.

MS is an important neurologic illness among veterans both in the number of veterans with the disease and the severity of resulting disability. Our veterans with MS deserve a vigorous VA research program. The articles in this special issue devoted to MS reveal the array of research being conducted by VA investigators and point to avenues where the MSCoEs can provide training, support, and a rich source of data to veterans and their providers.

REFERENCES

1. Multiple Sclerosis Centers of Excellence [homepage on the Internet]. Seattle: Department of Veterans Affairs; c2006 [updated 2006 Apr 20; cited 2004 Feb 27]. Description of VHA MS Cohort. VHA utilization and VHA expenditures: Preliminary analyses; [about 42 pages]. Available from: http://www.va.gov/ms/media/vha_mscoe_descriptive_report_year1_feb27_2004_1.doc

2. Bourdette DN, Prochazka AV, Mitchell W, Licari P, Burks J. Health care costs of veterans with multiple sclerosis: Implications for the rehabilitation of MS. VA Multiple Sclerosis Rehabilitation Study Group. Arch Phys Med Rehabil. 1993;74(1):26–31. [\[PMID: 8420515\]](#)
3. Vollmer TL, Hadjimichael O, Preiningerova J, Ni W, Buenconsejo J. Disability and treatment patterns of multiple sclerosis patients in United States: A comparison of veterans and nonveterans. J Rehabil Res Dev. 2002;39(2): 163–74. [\[PMID: 12051461\]](#)
4. Wagner EH. Chronic disease management: What will it take to improve care for chronic illness? Eff Clin Pract. 1998;1(1):2–4. [\[PMID: 10345255\]](#)
5. Wagner EH, Austin BT, Von Korff M. Organizing care for patients with chronic illness. Milbank Q. 1996;74(4): 511–44. [\[PMID: 8941260\]](#)

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