

## GUEST EDITORIAL

### Multiple sclerosis: Paradox and public policy\*

Multiple sclerosis (MS) is a frightening and devastating illness for many patients. Simultaneously, it is a fascinating biological puzzle that has attracted scientists from a wide variety of disciplines. Frightening and fascinating at once: that paradox has drawn many talented individuals into the field. Readers of this special single-topic issue of the *Journal of Rehabilitation Research and Development*, edited by Dr. Timothy Vollmer, will discover that the boundaries of rehabilitation in MS are being considerably expanded by advances in biology and technology and by our understanding of the pathogenesis of the illness. Many of the advances have been brought about by VA investigators. I would like to offer my personal view of the evolution of clinical care and research in MS over the past three decades. I will conclude with a consideration of public policy.

#### Clinical Care

For the afflicted individual, there is the ever-present uncertainty of when the illness will attack or accelerate next—the “Sword of Damocles.” MS often strikes at men and women who are embarking on families and careers and has a significant ripple effect on families. As “thecrippler of young adults,” MS has a powerful effect on public consciousness. What the general public does not usually see are the individual examples of personal fortitude and courage demonstrated by persons with MS and of the intense loyalty of caregivers.

MS has had great advances in clinical care and therapeutic interventions. Notable among these are the immunomodulating therapies that have cut down the relapse rate by 30 percent. Symptomatic therapies directed at bladder control, spasticity reduction, pain management, and antidepressants have contributed enormously to improving the day-to-day quality of life. The diagnosis and evaluation of therapeutic interventions took a leap forward with the introduction of magnetic resonance technology.

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\*The views expressed in this editorial do not purport to be the official policy of the Department of Veterans Affairs (VA).



**John Booss, MD**

*National Director, Neurology Service, Department of Veterans Affairs, Professor of Neurology and Laboratory Medicine, Yale University School of Medicine, New Haven, CT*

Hope now resides in cutting-edge rehabilitative therapies and computer-guided aids to enhance function. Dr. Vollmer's group has pioneered cell transplantation to remyelinate and reconstitute function. A brave new world indeed!

#### Pathogenesis Research

For many years, and continuing to this day, the Holy Grail of MS research has been to find the cause of MS. Histopathological findings of demyelination with inflammation led many investigators to suspect an infectious cause. That view received support from epidemiological studies, suggesting an environmental effect. There was precedent in acute disseminated encephalomyelitis (ADEM) a parainfectious process in which demyelination with inflammation in the central nervous system (CNS)

followed an apparently benign self-limited systemic infectious disease. Measles, prior to the era of vaccination, was a common precipitant of ADEM and a candidate virus for the cause of MS. Demonstration of persistent viral infection as the cause of chronic diseases of the nervous system included two disorders with demyelination. Children with subacute sclerosing panencephalitis (SSPE) were shown to harbor a defective measles virus in the brain. Similarly, a papova virus was shown to be the cause of demyelination in immunosuppressed persons with progressive multifocal leukoencephalopathy (PML). The concept of chronic viral infection was strengthened by the study of a demyelinating disease in sheep, Visna, caused by a retrovirus in the Lentivirus family. However, despite intensive work by many laboratories on numerous infectious agents, with interest continuing in Human Herpes Virus Six (HHV-6) and Epstein-Barr Virus (EBV), the general scientific community has not accepted a single infectious agent as the cause of MS.

The fact of finding antiviral antibodies in the cerebrospinal fluid (CSF) against numerous viruses, in addition to immunoglobulin of undetermined antigenic specificity and the presence of CSF specific oligoclonal bands also of undetermined antigenic specificity, supported the notion that MS might be an autoimmune disease. The immunopathology demonstrates an array of lymphocyte subtypes at crucial locations, such as in the perivascular space and at the edge of the demyelinating lesion. Support also came from studies of experimental allergic encephalomyelitis (EAE), perhaps the best studied of all experimental models of autoimmune disease. As with the chronic viral hypothesis, however, an exact delineation of the immunopathogenesis of MS has remained elusive.

A third piece of the pathogenesis puzzle is the contribution of the genetic makeup, which has long been apparent. Most convincingly, the prevalence of MS in first order relatives of persons with MS is significantly greater than that in matched control populations. Here, too, no simple explanation has been found. Instead, a multigene pattern of susceptibility has been found, particularly including the major histocompatibility complex. Taken together, epidemiologic, immunopathologic, and genetic studies support—but haven't proven—an MS pathogenesis

based on genetic susceptibility and an immunopathologic expression. The triggering event may be a response to one or more environmental triggers at a crucial time in immunologic and CNS development.

### **Public Policy**

Let me briefly consider public policy because of the fundamental importance of resource allocation for research and for assistance of persons with MS. Over the years, the National Multiple Sclerosis Society has done an excellent job portraying the plight of the person with MS and emphasizing the need for research funding. Recently, Democrats and Republicans in both houses of Congress have worked together toward doubling the biomedical research budget at the National Institutes of Health (NIH). VA has had a number of research initiatives for MS.

These organizational efforts have significantly increased the research opportunities to modify the clinical manifestations and to unravel the basic pathogenesis of MS. However, much remains to be done to establish integrated systems of high-quality care and to provide for basic needs of afflicted persons. The American healthcare nonsystem is a patchwork quilt of services characterized in the main by discontinuities. As a chronic illness, the full gamut of integrated services is needed for persons with MS, including diagnosis, disease management, symptom management, provision of medications and prosthetics, income maintenance, and health and personal services in a variety of settings. The Consortium of MS Centers is a forum in which the delivery of such services can be promulgated. The Department of Veterans Affairs is the only national system to provide the full range of services with continuity. Veteran service organizations such as the Paralyzed Veterans of America (PVA) and Eastern Paralyzed Veterans of America (EPVA) have been strong advocates for improved care of veterans with MS and for more research. Following congressional direction, VHA will establish two National MS Centers of Excellence for veterans. The intent of the centers will be to enhance the clinical care of all veterans with MS; educate patients, families, and healthcare providers; establish models of clinical care; and support innovative research. Extensive use of informatics and telemedicine will be intended to extend services to veterans nationwide.

**Concluding Remarks**

Many fundamental issues are unresolved for persons with MS. These include prescription drug coverage, access to affordable private insurance, and long-term care. The National Multiple Sclerosis Society and the American Academy of Neurology have worked individually, together, and in coalitions of like-minded organizations to bring

these issues before elected representatives at the state and federal level. Patients and their families, working with these organizations, are the most knowledgeable citizens with respect to MS and have great credibility when informing elected representatives.

*John Booss, MD*