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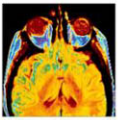

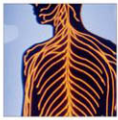
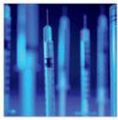

Multiple Sclerosis

Clinician's Guide to Diagnosis and Treatment

2nd Edition

GARY L. BIRNBAUM, M.D.

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Clinician's Guide to Diagnosis and Treatment

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Needless to say, my wife, daughter, and her family supported my efforts and indulged me the time away from them to write this book. I thank them too.

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Gary Birnbaum, MD

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Introduction

Many books have been written on the pathology, immunology, diagnosis, and treatment of persons with multiple sclerosis (MS). Most of these have been directed at neurologists and other specialists in the field, with details commensurate with the expertise of these readers. This book has a different purpose. Its goal is to present a practical and reasonable approach to the diagnosis and treatment of MS to those health professionals most likely to first see persons with MS, namely primary care physicians and clinical nurse specialists. The long-term care of persons with MS often is dependent on the expertise of such non-neurologists, but with the multitude of other illnesses cared for by primary care health professionals, providing a compendium of all known information about MS is not useful. Rather, I hope that this book will provide an algorithm for the diagnosis and treatment of persons with MS, as well as providing a foundation for more detailed readings on the subject.

As is quickly apparent at any meeting of MS experts, there is no one way to manage persons with MS. The variability in disease presentation, disease course, and variety of symptoms mandates an individualized approach. The approaches to be described in this book are those I have found useful over more than thirty years of caring for persons with MS. I don't espouse them as being the only way, but I hope they will serve as a framework for providing the best possible care to our patients.

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Chapter 1

A Brief History of Multiple Sclerosis

It is not possible to define the biological onset of a disease characterized not only by a particular clinical course but also by particular changes in the central nervous system (CNS; brain and spinal cord), since the technology necessary to look at changes in the CNS was not available until the late 19th century. However, by interpreting biographies and diaries of persons with symptoms suggestive of MS, it is possible to conjecture that MS historically occurred as early as the 14th century.

In a biography of St. Lidwina of Schiedam, symptoms suggestive of a fluctuating, multifocal neurologic illness are described that started in the year 1396 after ice skating. Her subsequent course of increased walking difficulties, with episodes that may have been remissions, suggests that she may have had similar to MS, though this is far from certain. St. Lidwina was canonized in 1890 and is now the patron saint of skaters.

A more robust description of symptoms strongly suggestive of MS is found in the diary of Sir Augustus Frederick d'Este (1794–1848), a grandson of England's King George III. In it he describes exacerbating remitting symptoms suggestive of optic neuritis and double vision, leg weakness, and bowel and bladder difficulties, followed over the years by gradually progressive weakness and spasms that left him bed-bound by the end of his life.

Why is a history of MS put into a book that is meant to be a primer on the diagnosis and care of persons with MS? For two reasons. One is to put into historical context the fact that MS occurred before the appearance of many modern toxins that have been impugned as causes of MS. These include mercury amalgam in tooth fillings (first used in the early 20th century) and environmental lead. That does not mean that environmental factors are unimportant in MS: as will be described in Chapter 2, environmental factors play a major role in disease susceptibility. Rather, in the absence of proof implicating a particular factor, great caution should be used in recommending any "treatments" based on unsupported hypotheses, such as advising persons with MS to have their dental amalgams removed or be detoxified with treatments such as chelation therapy. The second reason for having this chapter is to put into historical context the fact that any treatment for a disease such as MS, which can spontaneously remit, will in some instances appear successful. Many of the treatments received by Sir d'Este, such as bloodletting, leeches to the temples, beefsteaks twice a day, sherry and Madeira wine, rubbing with horsehair gloves, and undergoing a course of electricity, were associated with significant improvement and certainly would have been considered successful therapies by the physicians of that time.

While MS was not recognized as a distinct disease until 20 years after d'Este's death, pathologic descriptions of diseased brain were being made with

increasing frequency. A professor of anatomy, Robert Carswell, in 1838 was the first to note patches of hardened areas of scarring in the brain and spinal cord of persons who now would be classified as having MS. However, there were no clinical correlations. Working independently, the anatomist Jean Cruveilhier (1791–1894), in a book published in 1841, described multifocal areas of scarring in the brain and spinal cord. Cruveilhier was the first person to correlate the pathologic changes with symptoms such as tremors and walking difficulties.

The Parisian neurologist Jean-Martin Charcot (1825–1893), with his colleague Edmé Vulpian, in a series of lectures in 1868 was instrumental in summarizing the observations of the anatomists and defining MS as a separate clinical entity. He also described both demyelination and axonal loss as characteristic pathologic features of the disease. It is said that Charcot saw fewer than 40 cases of MS in his lifetime, including his maid, whom he believed had this illness, and thus considered it rare. Nevertheless, his careful clinical and pathologic observations laid the foundation for much of the work on MS in the subsequent century.

Research into the epidemiology of MS around the world was accelerated by the efforts of the Association for Research in Nervous and Mental Diseases (ARNMD) in 1921, leading to the observations of Lord Russell Brain, who in 1930 was one of the first to describe the uneven geographic distribution of MS.

Experimental Autoimmune Encephalomyelitis

While MS is an exclusively human disease, much of our understanding of autoimmune phenomena in the CNS is based on an animal model initially called experimental allergic encephalomyelitis (EAE). EAE was, induced by Thomas Rivers in 1935 following immunization of animals with CNS components. While there are major differences between MS and EAE, rodent EAE continues to be used as a model for MS and is used to establish "proof of concept" for potential treatments for MS. Indeed, all current therapies for MS were initially studied in EAE and were shown to be effective before being tested in humans. It is unlikely a therapy in this day and age would ever enter clinical trials without showing prior efficacy in ameliorating EAE. However, the majority of effective treatments of EAE have not proven to be effective when tested in human clinical trials.

EAE has also been useful in helping elucidate some of the presumed mechanisms of action of the disease-modifying therapies, described in Chapter 8. However, since this book is intended to be a practical compilation of data allowing health care providers to provide the best possible care to persons, rather than a compendium of information on all aspects of autoimmune central nervous system disease, a detailed description of changes in EAE induced by disease-modifying therapies is not be presented.

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