Clinical Neuroimmunology
Clinical Neuroimmunology

Multiple Sclerosis and Related Disorders

Edited by

Syed A. Rizvi, MD
Associate Professor of Neurology (Clinical)
Department of Clinical Neuroscience
Brown University
Providence, RI, USA

Patricia K. Coyle, MD
Professor and Acting Chair
Department of Neurology
Stony Brook Medical Center
East Setauket, NY, USA
The role of the immune system in the pathophysiology of neurological disorders is a topic of longstanding interest among clinicians and investigators in the field. As stated by Drs Rizvi and Coyle, editors of *Clinical Neuroimmunology: Multiple Sclerosis and Related Disorders*, much new information has accumulated in recent years which is beginning to influence the diagnosis and treatment of many of these disorders. This book serves the very useful purpose of making recent important developments in the field accessible, as well as understandable, to the general neurologist dealing with these disorders in the clinic.

The volume begins with a thorough overview of neuroimmunology and targeted immunotherapies followed by several chapters on the genetics, immunology, epidemiology, clinical and laboratory features, and treatment of multiple sclerosis. Subsequent sections deal with inflammatory disorders of the central nervous system, immune-mediated disorders of the peripheral nervous system, and systemic disorders with presumed autoimmune manifestations which affect the central and peripheral nervous system. Particular topics which are often not emphasized elsewhere are pediatric multiple sclerosis, the immunology of cortical diseases, and immunological aspects of movement disorders. Other chapters deal with the topical issues of neuromyelitis optica and the question of whether there is evidence for a vascular basis of multiple sclerosis. Of particular interest is the chapter by Dr. Howard Weiner predicting that the next 20 years in multiple sclerosis research will provide new and more effective treatments of progressive forms of multiple sclerosis, better biomarkers and an improved understanding of nervous system repair. The reader of this volume will discover that the quantity of knowledge gained in recent years is worthy of this new and comprehensive summary of the field.

Daniel Tarsy, MD
Beth Israel Deaconess Medical Center
Harvard Medical School
Boston, MA
Immune activation of the central or peripheral nervous system (CNS or PNS) has been shown to play a key role in the pathogenesis of many neurological disorders. Basic concepts in Clinical Neuroimmunology have changed significantly during the last 10 years, and are constantly evolving. New data has driven treatment concepts for a large number of autoimmune diseases, none more so than multiple sclerosis. As this area of research has become increasingly active and productive, the need for a comprehensive up-to-date handbook has become apparent.

Clinical Neuroimmunology: Multiple Sclerosis and Related Disorders has been written with the clinician in mind and targets residents, fellows, internists, nurse practitioners, as well as general neurologists. The aim of this book is to make recent developments in neuroimmunology accessible to the clinician who feels daunted by such advances, and requires a clear explanation of the scientific and clinical issues. The chapters have been written by experts in their fields. The introduction, Part I is written by Patricia K. Coyle and Lloyd Kasper and provides a logical and straightforward overview of neuroimmunology. Part II consists of eight chapters focused on multiple sclerosis. It includes a chapter on Chronic Cerebrospinal Venous Insufficiency (CCSVI), a topic currently getting a great deal of attention in the media. CCSVI is under investigation for its possible association with MS. Another chapter written by Howard Weiner envisions MS 20 years in the future. Part III has seven chapters and focuses on other CNS inflammatory disorders including neuromyelitis optica, ADEM, CNS infections, and immunological aspects of cancer. Part IV includes two chapters that describe autoimmune disorders of the PNS. The final (V) part includes a single chapter that focuses on various systemic diseases with prominent autoimmune CNS and PNS manifestations such as Behcet’s disease, Sarcoidosis, and Systemic Lupus Erythematosus. We hope health professionals who are interested in neuroimmunological disorders will find this book useful.

Finally, we would like to thank our contributing authors, for their hard work and guidance.

Providence, RI
Syed A. Rizvi
Stony Brook, NY
Patricia K. Coyle
# Contents

1. Introduction to Neuroimmunology ............................................................. 1  
   *Patricia K. Coyle*

2. Principles of Immunotherapy ................................................................. 15  
   *Jennifer L. Joscelyn and Lloyd Kasper*

## Part I  Multiple Sclerosis

3. MS: Pathology and Immunology ............................................................. 43  
   *Patricia K. Coyle*

4. MS: Epidemiology and Genetics ............................................................ 71  
   *Robert H. Gross and Philip L. De Jager*

5. MS: Clinical Features, Symptom Management, and Diagnosis ................. 89  
   *James M. Sankiewicz and Guy J. Buckle*

6. Advances in Magnetic Resonance Imaging of Multiple Sclerosis ................ 111  
   *Robert Zivadinov*

7. Disease Modifying Agents in the Treatment of Multiple Sclerosis .............. 131  
   *Syed A. Rizvi*

8. Pediatric Multiple Sclerosis ..................................................................... 157  
   *Lauren Krupp, Yashma Patel, and Vikram Bhise*

9. Is Multiple Sclerosis a Vascular Disease? ............................................. 179  
   *Mahesh V. Jayaraman and Syed A. Rizvi*

10. Multiple Sclerosis: The Next 20 Years ............................................... 191  
    *Howard L. Weiner*
Part II  Other CNS Inflammatory Disorders

11. Acute Disseminated Encephalomyelitis ................................. 203
   Patricia K. Coyle

12. Neuromyelitis Optica Spectrum Disorders .............................. 219
   Dean M. Wingerchuk

13. The Neuroimmunology of Cancer ......................................... 233
   Enrico C. Lallana, William F. Hickey, and Camilo E. Fadul

   Najam Zaidi, Melissa Gaitanis, John N. Gaitanis,
   Karl Meisel, and Syed A. Rizvi

15. The Neuroimmunology of Cortical Disease
   (Dementia, Epilepsy, and Autoimmune Encephalopathies) .......... 275
   Julie L. Roth, Brian R. Ott, John N. Gaitanis,
   and Andrew S. Blum

16. Autoimmune Movement Disorders ......................................... 291
   Victoria C. Chang

17. CNS Vasculitis ....................................................................... 307
   David S. Younger and Adam P.J. Younger

Part III  Peripheral Nervous System Disorders

18. Immunologic Disorders of Neuromuscular
    Junction and Muscle .............................................................. 333
    Kara A. Chisholm, James M. Gilchrist, and John E. Donahue

19. Autoimmune Neuropathies .................................................... 349
    George Sachs

Part IV  Systemic Disorders

20. Systemic Autoimmune Diseases with
    Neurological Manifestations .................................................. 375
    Richard Choi, Valarie Gendron, Mac McLaughlin,
    Jonathan Cahill, Fathima Qadeer, and Syed A. Rizvi

Index ................................................................................................ 391
Contributors

Vikram Bhise
Department of Neurology, Stony Brook University Medical Center,
Stony Brook, NY, USA

Andrew S. Blum, MD, PhD
Comprehensive Epilepsy Program, Department of Neurology,
Rhode Island Hospital, The Warren Alpert Medical School at Brown
University, Providence, RI, USA

Guy J. Buckle, MD
Partners MS Center, Brigham & Women’s Hospital,
Harvard Medical School, Brookline, MA, USA

Jonathan Cahill, MD
UMASS Medical School, Worcester, MA, USA

Victoria C. Chang, MD
Department of Medicine, Division of Neurology, Providence VA Medical
Center, Providence, RI, USA; The Movement Disorders Program,
Butler Hospital, Providence, RI; USA; Department of Clinical Neurosciences,
The Warren Alpert School of Medicine at Brown University,
Providence, RI, USA

Kara A. Chisholm, MD
Department of Neurology, Rhode Island Hospital, Warren Alpert Medical
School at Brown University, Providence, RI, USA

Richard Choi
Department of Neurology, Rhode Island Hospital, Providence, RI, USA

Patricia K. Coyle, MD
Professor and Acting Chair, Department of Neurology,
Stony Brook Medical Center, East Setauket, NY, USA
Contributors

John E. Donahue, MD
Department of Pathology, Division of Neuropathology, Rhode Island Hospital, Department of Pathology and Laboratory Medicine, Warren Alpert Medical School at Brown University, Providence, RI, USA

Camilo E. Fadul, MD
Neuro-Oncology Program, Norris Cotton Cancer Center, Departments of Medicine and Neurology, Dartmouth Medical School, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA

Melissa Gaitanis
Infectious Disease-Department of Medicine, Warren Alpert Medical School at Brown University, Providence, RI, USA

John N. Gaitanis
Department of Clinical Neurosciences, Warren Alpert Medical School at Brown University, Providence, RI, USA

Valarie Gendron
Department of Neurology, Rhode Island Hospital, Providence, RI, USA

James M. Gilchrist, MD
Department of Neurology, Rhode Island Hospital, Warren Alpert Medical School at Brown University, Providence, RI, USA

Robert H. Gross, MD
Department of Neurology, Center for Neurologic Diseases, Brigham & Women’s Hospital, Boston, MA, USA; Harvard Medical School, Boston, MA, USA; Partners Center for Personalized Genetic Medicine, Boston, MA, USA; Program in Medical & Population Genetics, Broad Institute of Harvard University and Massachusetts Institute of Technology, Cambridge, MA, USA

William F. Hickey, MD
Department of Pathology, Dartmouth Medical School, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA

Philip L. De Jager, MD, PhD
Department of Neurology, Center for Neurologic Diseases, Brigham & Women’s Hospital, Boston, MA, USA; Harvard Medical School, Boston, MA, USA; Partners Center for Personalized Genetic Medicine, Boston, MA, USA; Program in Medical & Population Genetics, Broad Institute of Harvard University and Massachusetts Institute of Technology, Cambridge, MA, USA

Mahesh V. Jayaraman, MD
Warren Alpert Medical School at Brown University, Interventional Neuroradiology, Rhode Island Hospital, Providence, RI, USA

Jennifer L. Joscelyn, MS
100 Merrimack Street, Hooksett, NH, USA

Lloyd Kasper
Dartmouth Medical School, Lebanon, NH, USA
Lauren Krupp
Department of Neurology, Stony Brook University Medical Center, Stony Brook, NY, USA

Enrico C. Lallana, MD
Neuro-Oncology Program, Norris Cotton Cancer Center, Departments of Medicine and Neurology, Dartmouth Medical School, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA

Mac McLaughlin, MD
UMASS Medical School, Worcester, MA, USA

Karl Meisel
Department of Neurology, Rhode Island Hospital, Providence, RI, USA

Brian R. Ott
Alzheimer’s Disease & Memory Disorders Center, Department of Neurology, Rhode Island Hospital, The Warren Alpert Medical School at Brown University, Providence, RI, USA

Yashma Patel
Department of Neurology, Stony Brook University Medical Center, Stony Brook, NY, USA

Fathima Qadeer, MD
Rhode Island Hospital, Providence, RI, USA

Syed A. Rizvi, MD
Associate Professor of Neurology (Clinical), Department of Clinical Neuroscience, Brown University, Providence, RI, USA

Julie L. Roth
Comprehensive Epilepsy Program, Department of Neurology, Rhode Island Hospital, The Warren Alpert Medical School at Brown University, Providence, RI, USA

George Sachs, MD, PhD
Alpert Medical School of Brown University, EMG Laboratory, Rhode Island Hospital, Providence, RI, USA

James M. Stankiewicz, MD
Partners MS Center, Brigham & Women’s Hospital, Harvard Medical School, Brookline, MA, USA

Howard L. Weiner, MD
Partners Multiple Sclerosis Center, Center for Neurologic Diseases, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA

Dean M. Wingerchuk, MD, MSc, FRCP(C)
Division of Multiple Sclerosis and Autoimmune Neurology, Mayo Clinic College of Medicine, Scottsdale, AZ, USA

David S. Younger, MD
Department of Neurology, New York University School of Medicine, New York, NY, USA
Adam P.J. Younger, MD
College of Arts and Sciences, Case Western Reserve University,
Cleveland, OH, USA

Najam Zaidi, MD
Warren Alpert Medical School at Brown University, Providence, RI,
USA and Department of Medicine, Kent Hospital, Warwick, RI, USA

Robert Zivadinov, MD
Department of Neurology, Buffalo Neuroimaging Analysis Center,
The Jacobs Neurological Institute, State University of New York, Buffalo,
NY, USA