Neurotropic Viral Infections

Neurotropic viruses infect the brain, often causing lethal disease in people. These diseases range from polio, to rabies and AIDS. This book is a depiction of each of these individual viruses. It discusses the diseases they cause, the mechanisms by which they cause and spread those diseases, the detection and treatment of these illnesses, and their prevention. There is also discussion of novel and beneficial uses of these neurotropic viruses for gene therapy and tumor lysis. It has been written in a style that is appealing for a very wide professional audience, ranging from graduate students, to postdocs, scientists, clinicians, and public health professionals.

Carol Shoshkes Reiss is a Professor in the Department of Biology at New York University. She was Editor-in-Chief of Viral Immunology from 1999–2006.

“. . . a cohesive and comprehensive overview of viral infection(s) of the nervous system . . . destined to become a great reference and text for some time to come.”

Michael J. Goldblatt President and CEO, Functional Genetics, Inc.

“The authors did an amazing job of walking that fine line between too much detail for non-specialists and not enough sophistication for the cognoscenti.”

Richard M. Ransohoff Director, Neuroinflammation Research Center

“I can’t imagine a better place to learn than this very well-thought out and comprehensive volume by leading authorities on this important subject.”

Stephen S. Morse Founding Director, Center for Public Health Preparedness, NCDP
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Foreword

Howard Lipton

*Neurotropic Viral Infections* is a timely compendium of reviews by noted experts in the field of neurotropic viruses, which cause serious neurological disease in humans. It is timely for a number of reasons. First, it is timely because an increasing number of stories of neurotropic virus infections have played out in the world news over the past decade. These include the spread of West Nile virus infection to New York State and across the North American continent; the emergence in Malaysia of two new paramyxoviruses that cause fatal encephalitis; the resurgence of paralytic poliomyelitis in sub-Saharan Africa as the WHO campaign to eradicate poliovirus mopped up the remaining cases; the sudden outbreak of Chikungunya fever, an alphavirus with neurological potential, in the Southwest Indian Ocean and India; the threat of mad cow disease spreading across the border from Canada into the Western United States; the surprising occurrence of progressive multifocal leukoencephalopathy (PML) in several multiple sclerosis patients and a Crohn’s disease patient treated with a powerful new immunosuppressive agent, Natalizumab (Tysabri™), a humanized monoclonal antibody against the integrin α4 on lymphocytes; and, finally, from a therapeutic standpoint, the marketing of a new varicella-zoster virus (VZV) vaccine that promises to substantially reduce the risk of painful shingles in the elderly, as well as the first successful treatment of a young girl with rabies encephalitis in Fond du Lac, Wisconsin. Second, the

1 Including prion diseases.
continuing HIV-AIDS epidemic and its neurological sequelae and rampant measles virus infections in Africa continue to be of great international concern. Third, the success of genotypic approaches to new virus discovery are being applied to neurological diseases of suspected viral etiology. Finally, the unrelenting (dizzying) progress in the biomedical sciences has had a profound impact on the conduct of research into the pathogenesis of all classes of neurotropic viruses, including the host immune response to these agents.

This book covers the gamut of neurotropic virus infections and is divided into five sections. The first section covers neurotropic RNA viruses causing human disease and includes chapters on such classic infections as poliomyelitis, subacute sclerosing panencephalitis, and rabies; chapters on West Nile, and Japanese B, encephalitides, as well as chapters on other infections.

Retroviral diseases – Human T-lymphotropic virus-1 (HTLV-1) and human immunodeficiency virus encephalitis – and several neurotropic DNA virus infections, such as PML and nervous system involvement by varicella-zoster and herpes simplex viruses and, in addition, transmissible spongiform encephalopathies are the focus of the second section.

Innate immunity in response to neurotropic virus infections is covered in the third section. The section includes chapters on Toll-like receptors and vaccines, as well as how the hypothalamic-pituitary-adrenal axis (i.e., neuro-endocrine networks), influences host immune responses. In addition, the third section of the book covers clinical aspects of neurotropic virus infections and includes chapters on the epidemiology of viral encephalitis, the clinical management of viral encephalitis, infectious disease discovery, and viral oncolysis of glioblastoma multiforme. Because many neurotropic virus infections are spread to humans by arthropod vectors and by bats, chapters on the ecology of vectors, virus-vector life cycles, and interventions are included in this section.

Clearly, viral infections of the brain remain one of the most frightening and mysterious of all human maladies. A better understanding of neurotropic viruses is still needed, and the time is propitious to update our knowledge in this area.
Preface and Acknowledgments

The idea for this book came from Martin Griffiths of Cambridge University Press, who approached me in October 2005. My initial reaction had been that I was too busy to undertake this project. I surprised myself by taking up the challenge. After giving the choice of topics and potential investigators much thought, I contacted the authors whose contributions you see here. Contracts from the Press were circulated in early 2006, and the manuscripts were submitted in the Spring of 2007, except by one very eager team, who completed their paper in October 2006.

We have attempted, in this volume, to put together a comprehensive survey of the principal viruses that cause disease in the central nervous system, the mechanisms by which they cause pathology and evade host responses, the host responses to these infections, and the tools available for diagnosis and treatment of the infections. Vaccine strategies, drug development, and the important questions concerning investigators and clinicians today are described. Given the rapid appearance of new agents and accompanying diseases, and the power of the scientific community to design new tools, we expect this field to continue its rapid changes. The need to provide information in a compact and up-to-date format is essential for students, faculty, clinicians, and public health personnel.

I could not have written my own chapter without the luxury of time from teaching and committee work, made possible by a yearlong sabbatical leave from New York University. For this leave, I am very grateful to Gloria Coruzzi, Chair of Biology.
Preface and Acknowledgments

Dan Stein, Dean for Science; Dick Foley, Dean of the Faculty of Arts and Sciences; and David McLaughlin, Provost. Passing along the responsibility for the Editor-in-Chief position of *Viral Immunology*, after 7 years of devotion, to David Woodland also freed me from other professional obligations during this period.

At Alice Huang's suggestion, I applied to the Rockefeller Foundation for a residency at its Villa Serbelloni in Bellagio on Lake Como in Italy and was privileged to be selected from among hundreds of applicants for an idyllic 4 weeks in May 2007. I am grateful to Tom Braciale, Peter Openshaw, and Peter Doherty, who wrote letters of support for the application. It is there at Bellagio, in the incredible Lombard setting, where the editing of the book was accomplished.

I was able to walk the steep hills to think, engage the fantastic minds of other residents and their accompanying people, and focus almost exclusively on this project.

In this book, as in all of my professional work, the contributions of my students and postdocs as well as my collaborators and other professionals who freely exchanged their findings and thoughts, critiques, suggestions, and comments, have been enormously important. I am also grateful for the support and encouragement of my sons, Steven and Joshua Reiss, and for my parents, Lila and Milton Shoshkes.

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