

New Concepts in the Immunopathogenesis of CNS Infections

Edited by Phillip K. Peterson and Jack S. Remington

The notion that the brain is an "immunoprivileged site" has been a major impediment to understanding the true importance of the immune system in the pathogenesis of CNS infections. In medical school, we learned about the blood-brain barrier, which limits the entry of inflammatory cells and molecules into the CNS, about the low levels of expression of major histocompatibility antigens on CNS cells, and about the absence of resident lymphocytes within the brain parenchyma. Yet few of us learned about the complex nature of immune responses that do occur in response to CNS infections. Not only do lymphocytes from the circulation enter the brain, but the resident cells of the brain upregulate the expression of the major histocompatibility complex and release numerous immune mediators. Although the primary purpose of this orchestrated immune reaction may be to fend off foreign invaders, an untoward consequence may be the injury of neurons and other brain cells.

Infections of the brain are widespread, especially in the setting of HIV infection, and they often have devastating, if not life-threatening, consequences. Understanding the complex interplay between specific CNS infectious agents and the immune response is critical if we are to unravel the pathogenesis of CNS infections and develop new strategies to control them. The book under review is an important step in this direction. It is a "state-of-the-art" description of our present knowledge about general features of the immune response in the CNS and about specific features relating to host defense against individual CNS pathogens. In the first part of the book, basic principles of neuroimmunology are reviewed, and there are chapters that focus on the entry of cells into the CNS, the immunomodulatory roles of astrocytes and microglia, and the role of cytokines and chemokines in the host's CNS defense.

In the second section of the book, major clinical and experimental CNS infectious syndromes are discussed, including the following: bacterial meningitis, tuberculous meningitis, neurologic Lyme disease, CNS toxoplasmosis, cryptococcal meningitis, herpes simplex encephalitis, progressive multifocal leukoencephalopathy, prion diseases, alphavirus encephalomyelitis, and infection with simian immunodeficiency virus, Borrelia disease virus, or Theiler's virus. In the final two chapters of the book, neurologic diseases of noninfectious etiology are discussed, including multiple sclerosis and neurodegenerative diseases.

This book arose from a meeting in October 1999 that brought together a group of 20 experts to discuss topics related to the immunopathogenesis of infections of the brain. The organizers of the meeting are the editors of the book, and the invited speakers are the authors of the individual chapters; all are leading authorities in their fields. The expertise of the writers is one of the greatest strengths of this book. For the most part, each chapter contains a fairly comprehensive review of the most salient issues regarding the immunopathogenesis of the pathogen under consideration. However, there is not much uniformity among different chapters with respect to organization or focus. In part, this may be an inevitable consequence of including diverse topics for which there is wide variation in our level of understanding of immunopathogenetic mechanisms. In chapters that discuss human infections for which the molecular aspects of pathogenesis are poorly understood (e.g., neurologic Lyme disease and progressive multifocal leukoencephalopathy), the focus is on clinical descriptions, whereas in chapters that deal with experimental models of CNS infections, the focus is more on basic concepts of molecular immunopathogenesis.

Readers are cautioned that this book is a collection of interesting dissertations that has been inspired by a scientific meeting, not a comprehensive text on the subject of host-pathogen interactions in the brain. Consequently, not only do the organization and scope of individual chapters vary, but some critical subject areas are inadequately addressed. Surprisingly, for a book that was inspired by the editors’ particular interest in two forms of brain infection (CNS toxoplasmosis and HIV encephalopathy), strikingly little attention is devoted to neurologic disease caused by HIV infection. HIV infection is discussed indirectly in the introductory chapters, which discuss the principles of neuroimmunology, and macaque simian immunodeficiency virus neuropathogenesis models are discussed in a later chapter. However, given the medical importance of HIV encephalopathy, the extensive research done in recent years on the immunopathogenesis of this disease, and the consideration that HIV encephalopathy is arguably one of the best examples of CNS immunopathogenesis, at least one chapter should have been devoted specifically to neurologic HIV infection.

Despite this limitation, clinicians and researchers with a general interest in host-pathogen interactions in the brain will undoubtedly find this book of inter-

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rug Interactions in Infectious Diseases

By Stephen C. Piscitelli and Keith A. Rodvold


The development of potent antiretroviral agents for the treatment of HIV infection has stimulated renewed interest in the problem of drug interactions. The pharmacotherapy of infectious diseases has become increasingly complex because of polypharmacy, the introduction of new antimicrobial agents, and, especially, the numerous drug interactions associated with protease inhibitors and nonnucleoside reverse transcriptase inhibitors.

Drug Interactions in Infectious Diseases is, therefore, a very timely text. It includes a chapter on the mechanisms of drug interactions, followed by chapters on antiretroviral agents; drugs for treatment of HIV-related infections; antibiotic, antifungal, and antimycobacterial agents; food interactions; and cytokine interactions. The chapter on mechanisms gives a broad overview, with particular emphasis on the cytochrome P-450 enzyme system. The chapter on antiretroviral agents is thorough and includes several useful tables. Unfortunately, there are a few typographical errors in these tables. For example, the recommended dosage of efavirenz in combination with amprenavir plus ritonavir is given as 600 mg q.i.d.; it should be 600 mg q.d. Also, no information is included about lopinavir/ritonavir, a recently released protease inhibitor combination that interacts with many other drugs.

The chapter on drugs for treatment of HIV-related infections is particularly useful. The common and complex interactions between antimycobacterial, antifungal, antiviral, and other agents are clearly illustrated. In this chapter, the tables include reasonable alternative management options for patients who require treatment with agents that interact.

The chapters on other antimicrobial agents are fairly comprehensive. Several interactions between commonly used antibiotics, including some with potentially serious consequences, are emphasized. Even Infectious Diseases (ID) specialists might not be aware of some of these interactions. Most of the tables in these chapters are quite thorough, with a few exceptions. For example, warfarin is not included in the table of drugs that interact with itraconazole. Nevertheless, these chapters contain a good amount of information that will be useful to ID clinicians.

The chapter on food interactions tabulates recommendations for administration of all anti-infective agents, with or without food. Finally, the chapter on cytokine interactions discusses the effect of alterations in cytokine levels on drug pharmacokinetics. Alterations in cytokine levels can occur as a result of infection, trauma, or vaccination. Alterations can also occur as a result of the direct administration of cytokines (e.g., interferons and interleukins). Although relatively few data are currently available on alterations in cytokine levels in humans, this problem is likely to become increasingly relevant as the clinical use of cytokines and anticytokine agents becomes more common.

The strengths of this book include its in-depth review of the mechanisms of pharmacokinetic and pharmacodynamic interactions and its attempt to provide approaches for managing the polypharmacy that is often required by patients with infectious diseases. Extensive tables are included in each chapter, and although they vary in quality, some are very useful. The weaknesses of the book include typographical errors, omissions from some of the tables, and the division of overlapping material into separate chapters. In addition, the usefulness of any book will be limited because new anti-infective agents are developed more rapidly than a book can be published; for example, this book has no information on lopinavir, linezolid, and telithromycin, which have become available in recent months. Clearly, computerized databases are likely to be the most useful resource for evaluating the rapidly changing myriad of potential interactions that patients face.

Nevertheless, these are minor criticisms of an interesting and extensively referenced book that should prove extremely helpful to pharmacists, pharmacologists, and medical educators. I believe this text can also benefit ID clinicians, as a useful reference and a review of the mechanisms of drug interactions, and it should heighten our awareness of this ever-growing problem.

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Handbook of Antibiotics, 3d Edition

By Richard E. Reese, Robert F. Betts, and Bora Gumustop
Philadelphia: Lippincott, Williams & Wilkins, 2000. 624 pp., illustrated. $39.95 (paper).

The soft-cover text Handbook of Antibiotics, 3d edition, is a convenient, midsize, practical review of infectious diseases and antibiotics. Initially published in 1983, this text has been a very popular addition to the clinician’s bookshelf. As indicated in the preface, the handbook is intended...