The Spectrum of Neuro-AIDS Disorders

Pathophysiology, Diagnosis, and Treatment
The Spectrum of Neuro-AIDS Disorders

Pathophysiology, Diagnosis, and Treatment

Edited by

Karl Goodkin, M.D., Ph.D., FAPA
Department of Psychiatry and Behavioral Neurosciences, Cedars-Sinai Medical Center, and Department of Psychiatry and Biobehavioral Sciences, University of California-Los Angeles, Los Angeles, California

Paul Shapshak, Ph.D.
Ann Lowerey Murphey Laboratory, Department of Psychiatry and Behavioral Medicine, University of South Florida College of Medicine, Tampa, Florida

Ashok Verma, M.D., D.M.
Department of Neurology, University of Miami Miller School of Medicine, Miami, Florida

ASM PRESS
Washington, DC
## Contents

Contributors / ix  
Preface / xiii  

### SECTION I  
**DISORDERS DUE TO PRIMARY HIV-1 PATHOGENESIS AND THEIR TREATMENT** / 1  

1. **HIV-1-Associated Neurocognitive Disorders in the HAART Era** / 3  
   KARL GOODKIN, AARON ARONOW, GAYLE BALDWIN, REBECA MOLINA, WENLI ZHENG, AND W. DAVID HARDY  

2. **Evolution of Neuropsychological Issues in HIV-1 Infection during the HAART Era** / 29  
   THOMAS D. MARCOTTE AND J. COBB SCOTT  

3. **HIV Infection and Stroke: the Changing Face of a Rising Problem** / 45  
   MAURICIO CONCHA AND ALEJANDRO RABINSTEIN  

4. **HIV-Associated Myelopathy, Myopathy, and Meningitis** / 57  
   LYDIA ESTANISLAO  

5. **Investigation and Presentation of Autonomic Neuropathies in HIV Infection** / 65  
   ROY FREEMAN AND RACHEL NARDIN  

6. **Distal Sensory Polyneuropathy and Other Selected Neuropathies in HIV Infection** / 75  
   LYDIA ESTANISLAO, ANTHONY GERACI, AND DAVID SIMPSON  

7. **Mitochondrial Dysfunction and Lactic Acidosis in HIV Disease** / 87  
   ASHOK VERMA AND JORGE PARDO  

8. **Neurologic Outcomes in HIV Infection: Clinical Events and Surrogate Markers** / 95  
   CONSTANTIN T. YIANNOUTSOS  

9. **Designing HIV gp120 Peptide Vaccines: Rhetoric or Reality for Neuro-AIDS** / 105  
   PANDJASSARAME KANGUEANE, RAJARATHINAM KAYATHRI, MEENA KISHORE SAKHARKAR, DARREN R. FLOWER, KRISTEN SADLER, FRANCESCO CHIAPPELLI, DAVID M. SEGAL, AND PAUL SHAPSHAK  

### SECTION II  
**PATHOPHYSIOLOGICAL ISSUES** / 121  

10. **Neurovirological Aspects of HIV Infection in the HAART Era** / 123  
    ZAHIDA PARVEEN, EDWARD ACHEAMPONG, ROGER J. POMERANTZ, AND MUHAMMAD MUKHTAR  

11. **Neuroimmunology and the Pathogenesis of HIV-1 Encephalitis in the HAART Era: Implications for Neuroprotective Treatment** / 137  
    SETH W. PERRY AND HARRIS A. GELBARD  

12. **Chemokines and the Neuropathogenesis of HIV-1 Infection** / 151  
    DAWN EGGERT, ERIC ANDERSON, JIALIN ZHENG, AND HOWARD E. GENDelman  

13. **Cerebrospinal Fluid Markers in the Management of Central Nervous System HIV Infection and the AIDS Dementia Complex** / 173  
    MAGNUS GISSSLÉN, LARS HAGBERG, PAOLA CINQUE, BRUCE BREW, AND RICHARD W. PRICE
14. The Neuropathology of HIV Pre- and Post-HAART / 181
JUTTA K. NEUENBURG

15. The Role of Viral Genetic Variability in HIV-Associated Neurocognitive Disorder / 201
PAUL SHAPSHAK, ALIREZA MINAGAR, PANDJASSARAME KANGUEANE, SIMON FROST, SERGEI L. KOSAKOVSKY POND, SELENE ZARATE, ELYSE SINGER, DEBORAH COMMINS, ANNE DE GROOT, MIGUEL QUINONES-MATEU, AND ERNEST TERWILLIGER

16. Antioxidants and Brain Function in HIV/AIDS / 219
GAIL SHOR-POSNER, ADRIANA CAMPA, MARIA-JOSE MIGUEZ-BURBANO, GLORIA CASTILLO, AND GERALDINE MORENO-BLACK

17. Cell Cycle Proteins and the Pathogenesis of HIV-1 Encephalitis in the HAART Era / 231
KELLY L. JORDAN-SCIUTTO AND CAGLA AKAY

SECTION III ___________________________
NEUROIMAGING IN HIV INFECTION / 245

18. The Uses of Structural Neuroimaging in the Brain in HIV-1-Infected Patients / 247
MAJDA M. THURNHER AND M. JUDITH DONOVAN POST

THOMAS ERNST, DARDO TOMASI, AND LINDA CHANG

20. Magnetic Resonance Spectroscopy in HIV-Associated Brain Injury / 281
LINDA CHANG, KAI ZHONG, AND THOMAS ERNST

SECTION IV _____________________________
HIV COMORBIDITIES / 293

MAREK RADKOWSKI, JONATHAN NASSERI, AND TOMASZ LASKUS

22. Toxoplasmosis of the Central Nervous System / 313
KATIA V. BROWN AND DANIEL J. SKIEST

23. Basic and Clinical Aspects of Human Cytomegalovirus Infection / 331
ROBERT R. McKENDALL AND ALEX TSELIS

24. Cryptococcosis and Other Fungal Infections of the Central Nervous System / 347
ROGER J. BEDIMO AND DANIEL J. SKIEST

25. Neurosyphilis in AIDS / 363
JOSEPH R. BERGER AND AARON J. BERGER

DAVID B. CLIFFORD

27. Epstein-Barr Virus Infection and Primary Central Nervous System Lymphoma / 383
ALEX TSELIS AND ROBERT McKENDALL

28. Mood Disorders, Delirium, and Other Neurobehavioral Symptoms and Disorders in the HAART Era / 393
STEPHEN J. FERRANDO AND TODD LOFTUS

29. Substance Use Disorders and Neuro-AIDS in the HAART Era / 411
JEFFREY A. RUMBAUGH AND AVINDRA NATH

SECTION V ________________________________
SPECIAL POPULATIONS AND NEURO-AIDS / 425

30. Ethnicity and Neuro-AIDS Conditions in the HAART Era / 427
LOYDA M. MELENDEZ, RAUL MAYO-SANTANA, CARLOS LUCIANO, AND VALERIE WOJNA

GABRIELE ARENDT, Y. JAEGER, AND TH. NOLTING

32. Pediatric Neuro-AIDS / 455
ANITA L. BELMAN

33. Interaction of the Aging Process with Neurobehavioral and Neuro-AIDS Conditions in the HAART Era / 473
KARL GOODKIN, MAURICIO CONCHA, BETH D. JAMIESON, ROSA REBECA MOLINA, ENRIQUE LOPEZ, WENLI ZHENG, DESHRATN ASTHANA, AND WILLIAM DAVID HARDY
SECTION VI  
SPECIAL HEALTH CARE ISSUES  
AND NEURO-AIDS  /  487

34. Neurologic Aspects of Palliative Care for HIV/AIDS  /  489
PETER A. SELWYN AND JOHN BOOSS

SOMA SAHAI-SRIVASTAVA

BRUCE J. BREW

Index  /  525
Contributors

EDWARD ACHEAMPONG
Dept. of Medicine, Thomas Jefferson University, Philadelphia, PA 19107

CAGLA AKAY
Dept. of Pathology, University of Pennsylvania, Philadelphia, PA 19104-6030

ERIC ANDERSON
Laboratory of Neuregeneration, Dept. of Pharmacology and Experimental Neuroscience, University of Nebraska Medical Center, Omaha, NE 68198-5880

GABRIELE ARENDT
Dept. of Neurology, University Hospital of Duesseldorf (UKD), Duesseldorf, Germany

AARON ARONOW
Dept. of Neurology, Keck School of Medicine, GNH 5641, University of Southern California, Los Angeles, CA 90033

DESHRATN ASTHANA
Laboratory for Clinical and Biological Studies, Dept. of Psychiatry and Behavioral Sciences, Fox Cancer Center, University of Miami, Miami, FL 33136

GAYLE BALDWIN
Dept. of Medicine, David Geffen School of Medicine, and UCLA AIDS Institute, University of California, Los Angeles, CA 90095

ROGER J. BEDIMO
Infectious Diseases Section, VA North Texas Health Care System, Dallas, TX 75216, and Division of Infectious Diseases, The University of Texas Southwestern Medical Center at Dallas, Dallas, TX 75390-9113

ANITA L. BELMAN
Dept. of Neurology, School of Medicine, Stony Brook University, Stony Brook, NY 11794

JOSEPH R. BERGER
Dept. of Neurology, University of Kentucky College of Medicine, Lexington, KY 40536

AARON J. BERGER
Division of Plastic Surgery, Stanford University, Stanford, CA 94305

JOHN BOOSS
Yale University School of Medicine and Virology Laboratories, VA Connecticut, New Haven, CT 06510

BRUCE BREW
Dept. of Neurology and Dept. of HIV Medicine, Centre for Immunology, and National Centre in HIV Epidemiology and Clinical Research, St. Vincent’s Hospital, University of New South Wales, Sydney 2010, Australia

KATIA V. BROWN
Division of Infectious Diseases, The University of Texas Southwestern Medical School, Dallas, TX 75390

ADRIANA CAMPA
Dept. of Dietetics and Nutrition, Florida International University, Stempel School of Public Health, Miami, FL 33199

GLORIA CASTILLO
Dept. of Epidemiology and Public Health, Division of Disease Prevention, University of Miami Miller School of Medicine, Miami, FL 33136

LINDA CHANG
Dept. of Medicine, Division of Neurology, University of Hawaii, John A. Burns School of Medicine, Honolulu, HI 96813

FRANCESCO CHIAPPELLI
Division of Oral Biology and Medicine, Laboratory of Human Oral and Molecular Immunology, UCLA School of Dentistry, University of California at Los Angeles, Los Angeles, CA 90095-1668

PAOLA CINQUE
Clinic of Infectious Diseases, San Raffaele Scientific Institute, Milano, Italy

DAVID B. CLIFFORD
Dept. of Neurology, Washington University School of Medicine, St. Louis, MO 63110
CONTRIBUTORS

DEBORAH COMMINS  
Dept. of Pathology (Neuropathology), University of Southern California Keck School of Medicine, Los Angeles, CA 90089

MAURICIO CONCHA  
Intercoastal Medical Group, Sarasota, FL 34232

ANNE DE GROOT  
EpiVax, Inc., and Biomedical Center, Brown University School of Medicine, Providence, RI 02912

DAWN EGGERT  
Laboratory of Neuregeneration, Dept. of Pharmacology and Experimental Neuroscience, University of Nebraska Medical Center, Omaha, NE 68198-5880

THOMAS ERNST  
Dept. of Medicine, Division of Neurology, University of Hawaii, John A. Burns School of Medicine, Honolulu, HI 96813

LYDIA ESTANISLAO  
Clinical Neurology Specialists, Las Vegas, NV 89146

STEPHEN J. FERRANDO  
New York-Presbyterian Hospital, Weill Medical College of Cornell University, New York, NY 10065

DARREN R. FLOWER  
The Jenner Institute, University of Oxford, Compton, Berkshire, RG20 7NN, United Kingdom

ROY FREEMAN  
Dept. of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215

SIMON FROST  
Antiviral Research Center, Dept. of Pathology, University of California San Diego, San Diego, CA 92103

HARRIS A. GELBARD  
Center for Aging and Developmental Biology, Kornberg Medical Research Institute, and Departments of Neurology, Pediatrics, Microbiology, and Immunology, University of Rochester Medical Center, Rochester, NY 14620

HOWARD E. GENDelman  
Laboratory of Neuotoxicology, Dept. of Pharmacology and Experimental Neuroscience, Center for Neurovirology and Neurodegenerative Disorders, University of Nebraska Medical Center, Omaha, NE 68198-5880

ANTHONY GERACI  
St. Luke’s-Roosevelt Hospital, New York, NY

MAGNUS GISSLÉN  
Dept. of Infectious Diseases, Göteborg University, Sahlgrenska University Hospital, Göteborg, Sweden

KARL GOODKIN  
Dept. of Psychiatry and Behavioral Neurosciences, Cedars-Sinai Medical Center, and Dept. of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, UCLA, Los Angeles, CA 90048

LARS HAGBERG  
Dept. of Infectious Diseases, Göteborg University, Sahlgrenska University Hospital, Göteborg, Sweden

W. DAVID HARDY  
Division of Infectious Diseases, Dept. of Internal Medicine, Cedars-Sinai Medical Center, and David Geffen School of Medicine, UCLA, Los Angeles, CA 90048

Y. JAEGAR  
Dept. of Surgery, Presbyterian Hospital of Duesseldorf, Duesseldorf, Germany

BETH D. JAMIESON  
UCLA Flow Cytometry Core Facility, Dept. of Medicine/Hematology-Oncology, UCLA, Los Angeles, CA 90048

KELLY L. JORDAN-SCIUTTO  
Dept. of Pathology, University of Pennsylvania, Philadelphia, PA 19104-6030

PANDJASSARAME KANGUEANE  
Biomedical Informatics, 17A Iulian Sundai Annex, Fondicherry 607402, India

RAJARATHNAM KAYATHRI  
Biomedical Informatics, 17A Iulian Sundai Annex, Fondicherry 607402, India

SERGEI L. KOSAKOVSKY POND  
Antiviral Research Center, Dept. of Pathology, University of California San Diego, San Diego, CA 92103

TOMASZ LASKUS  
St. Joseph’s Hospital and Medical Center, Phoenix, AZ 85013

TODD LOFTUS  
New York-Presbyterian Hospital, Weill Medical College of Cornell University, New York, NY 10065

ENRIQUE LOPEZ  
Dept. of Psychiatry and Behavioral Neurosciences, Cedars-Sinai Medical Center, and Dept. of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, UCLA, Los Angeles, CA 90048

CARLOS LUCIANO  
Dept. of Physical Medicine and Division of Neurology, NeuroAIDS Program, UPR, MSC, SNRP, University of Puerto Rico, Medical Sciences Campus, San Juan, PR 00936-5067

THOMAS D. MARCOTTE  
Dept. of Psychiatry, HIV Neurobehavioral Research Center, University of California, San Diego, San Diego, CA 92119

RAUL MAYO-SANTANA  
Dept. of Physical Medicine and Division of Neurology, NeuroAIDS Program, UPR, MSC, SNRP, University of Puerto Rico, Medical Sciences Campus, San Juan, PR 00936-5067

ROBERT R. McKENDALL  
Dept. of Neurology, Dept. of Microbiology and Immunology, University of Texas Medical Branch, Galveston, TX 77555
CONTRIBUTORS

DANIEL J. SKIEST
Adult HIV Program, Division of Infectious Diseases, Baystate Medical Center, Springfield, MA 01119, and Tufts University School of Medicine

ERNEST TERWILLIGER
Harvard Institute of Medicine, Boston, MA 02115

MAJDA M. THURNHER
Dept. of Radiology, Neuroradiology Section, Medical University of Vienna, Waehringer Guertel 18-20, 1090-Vienna, Austria

DARDO TOMASI
Medical Dept., Brookhaven National Laboratory, Upton, NY 11973

ALEX TSELIS
Dept. of Neurology, UHC-8D, Wayne State University, Detroit, MI 48201

ASHOK VERMA
University of Miami Miller School of Medicine, Miami, FL 33136

VALERIE WOJNA
Dept. of Physical Medicine and Division of Neurology, NeuroAIDS Program, UPR, MSC, SNRP, University of Puerto Rico, Medical Sciences Campus, San Juan, PR 00936-5067

CONSTANTIN T. YIANNOUTSOS
Dept. of Medicine, Division of Biostatistics, Indiana University School of Medicine, 410 West 10th Street, Suite 3000, Indianapolis, IN 46202

SELENE ZARATE
Dept. of Genetics, Independent University of Mexico City, San Lorenzo 290, Col. Del Valle, 03100 México, D.F., México

JIALIN ZHENG
Laboratory of Neurotoxicology, Dept. of Pharmacology and Experimental Neurosciences, Center for Neurovirology and Neurodegenerative Disorders, University of Nebraska Medical Center, Omaha, NE 68198-5880

WENLI ZHENG
Division of Enrollment Management, Market Research & Communications, University of Miami, Coral Gables, FL 33146

KAI ZHONG
Dept. of Biomedical Magnetic Resonance, Institute for Experimental Physics, Otto-von-Guericke-University Magdeburg, Leipziger Str. 44, Haus 01, D-39120 Magdeburg, Germany
Preface

The Spectrum of Neuro-AIDS Disorders: Pathophysiology, Diagnosis, and Treatment represents a compendium of knowledge that is unique to the field of neuro-AIDS. At this point in the era of highly active antiretroviral therapy (HAART), we have come to appreciate, more than ever before, the implications of the brain as an organ that becomes a reservoir for resistant HIV, contributing to a deleterious impact of this chronic infection on patient functioning. The book is designed to present a coordinated focus on the integration of knowledge regarding the pathophysiological bases, diagnostic approaches, and clinical treatment strategies specific for neuro-AIDS conditions in the HAART era today. Each chapter bridges the literature in its respective area from the former results in the pre-HAART era to the current knowledge base. Since HAART was introduced in late 1995, it has only recently become possible to present a consensus on changes in clinical outcomes such as those presented in this book. Hence, this book should be useful not only to clinicians but also to students and teachers in many areas.

As the morbidity and mortality of HIV infection have decreased greatly over the HAART era, neuro-AIDS conditions have shifted along with this change. Currently, the most prevalent neuro-AIDS condition is distal sensory polyneuropathy. Primary central nervous system (CNS) lymphoma is now a diagnosis of increased suspicion for mass lesions in the brain with respect to CNS toxoplasmosis, and iatrogenic neurological and neurobehavioral conditions due to prescribed medication toxicities have blossomed. The latter include the toxicities of the antiretroviral medications themselves. Efavirenz is the most widely cited antiretroviral regarding neurological and neurobehavioral outcomes of medication toxicity, including sleep disturbance, vestibular abnormalities, and neurocognitive impairment. However, long-term atherogenic risk, now attributed to HAART toxicity, has also changed the face of neuro-AIDS in the HAART era. A concern for such a vascular risk must now also be considered clinically, in addition to the damage to brain tissue caused both by HIV infection directly and by the inflammatory response to the presence of the virus. Thus, the entire neuropathogenic basis for understanding and defining these disorders has been altered. Moreover, in recognition of these changes, the diagnostic approach to several of the neuro-AIDS conditions, in particular the neurocognitive disorders, has evolved. Thus, a book of this magnitude is timely to integrate the changes noted in HIV-associated neuropathogenesis with associated changes in indicated diagnostic procedures and in treatment decision-making.

Section I of this book covers disorders due to primary HIV pathogenesis. At the outset, HIV-associated neurocognitive disorder (chapter 1, Goodkin et al.) and neuropsychological issues (chapter 2, Marcotte and Scott) are presented. This is followed by a presentation of a rising, long-term, antiretroviral toxicity concern, the risk of cerebrovascular accident (CVA, or stroke) (chapter 3, Concha and Rabinstein). Chapter 4 (Estanislao) presents HIV-associated meningitis, which is particularly frequent in the setting of acute conversion syndrome. Moving down the neuraxis, this chapter also includes HIV-associated myelopathy, radiculopathy, and myopathy. There is a separate presentation in chapter 5 (Freeman and Nardin) of autonomic neuropathies in HIV infection, which are much less frequently noted in clinical practice than their actual prevalence merits. Peripheral neuropathies are then presented in some detail in chapter 6 (Estanislao et al.), with the most common form, distal sensory polyneuropathy, followed by dideoxynucleoside-induced toxic neuropathy and other toxic neuropathies as well as inflammatory demyelinating polyneuropathy, mononeuropathy multiplex, and progressive polyradiculopathy.

A particularly important area of clinical concern being more closely examined at this point in the HAART era is centered predominantly upon an antiretroviral toxicity, mitochondrial dysfunction with lactic acidosis. Thus, mitochondrial dysfunction is presented in this section, with reference to lactic acidosis as the targeted clinical condition for diagnosis and treatment (chapter 7, Verma and Pardo). In fact, severe lactic acidosis can affect multiple organ systems, particularly the peripheral nerves and muscle (of relevance to neuro-AIDS conditions) as well as the liver, kidneys, and pancreas. Next, chapter 8 (Yiannoutsos) provides an overall view of how neuro-AIDS outcomes are best examined methodologically as clinical events with associated surrogate markers. The latter is a prominent current issue, as the utility of numerous surrogate markers for neuro-AIDS conditions in the pre-HAART era has become eroded or erased over the course of the HAART era. Finally, in chapter 9, Kangeue and al. consider the import of vaccine studies applied to neuro-AIDS conditions, a rapidly evolving area that brings us into the vista for the future.
Section II covers pathophysiological issues. First discussed are the neurovirological aspects of HIV infection in the HAART era (chapter 10, Parveen et al.). This is an area currently experiencing a resurgence of investigative interest compared to the historically greater focus devoted to neuroinflammatory mechanisms. Next, enhancing contrast, neuroimmunology, and neuroinflammation in the pathogenesis of HIV-1 encephalitis in the HAART era are covered, including novel implications for neuroprotective treatments (chapter 11, Perry and Gelbard). A more specific focus is then directed toward the chemokines in the neuropathogenesis of HIV infection (chapter 12, Gendelman and colleagues). A similar level of specific focus is devoted to the cerebrospinal fluid by a contribution representing several groups (chapter 13, Gisslén et al.). Chapter 14 (Neuenburg) examines the changes in the neuropathology of HIV infection, including work demonstrating the surprising increase in incidence of HIV encephalopathy in the HAART era. A specific note is also made therein of recent work supporting the pathophysiological importance of microbial translocation from the gastrointestinal tract.

The next contribution in section II presents a focus on the role of viral genetic variability in HIV-1-associated neurocognitive disorders (chapter 15, Shapshak et al.), acknowledging the growing interest in that area. Further, the role of antioxidants in HIV-associated infection of the brain is considered, together with therapeutic implications including nutritional interventions (chapter 16, Shor-Posner et al.). Section II concludes with a chapter on a novel pathogenic focus in neuro-AIDS that is currently gaining attention: cell cycle proteins (chapter 17, Jordan-Sciutto and Akay).

Section III considers the utility of selected neuroimaging techniques in HIV infection. The first chapter focuses on structural neuroimaging of the brain in HIV-infected patients (chapter 18, Thurnher and Post). This technique has been predominantly utilized for diagnosing and monitoring the treatment response of the complications of HIV infection of the brain (rather than for primary HIV-associated neurocognitive impairment and disorder). The roles of structural neuroimaging in CNS toxoplasmosis and primary CNS lymphoma diagnosis and therapeutic management are discussed in detail. Next in this section is a consideration of functional magnetic resonance imaging (fMRI), which includes a focus on blood oxygenation level-dependent fMRI (BOLD fMRI) (chapter 19, Ernst et al.). This technique can be used to increase the sensitivity with which HIV-associated neuropsychological impairment and disorder may be identified. For example, neuropsychological test challenges can be used with pre- and post-fMRI evaluation of adequacy of performance and identification of the types of abnormalities elicited in response. This neuroimaging technique may be particularly helpful for HIV-infected patients with comorbid psychoactive substance use disorders. The last chapter in this section is devoted to magnetic resonance spectroscopy (MRS) (chapter 20, Chang et al.). MRS provides quantified absolute concentrations of brain tissue metabolites that are region-specific and indicative of tissue damage. It is now recognized to be a useful diagnostic technique for a number of CNS complications of HIV infection as well as for HIV infection itself, the focus of this chapter. MRS is relevant not only to the diagnosis of HIV-associated neurocognitive impairment and disorder but also to the monitoring of treatment response. This noninvasive technique is gaining clinical recognition and is now reimbursable by some third-party payers. Overall, the neuroimaging section of this volume may be considered to provide bridges between section II on pathophysiological issues and the sections devoted to clinical manifestations (section I on disorders due to primary HIV pathogenesis, and section IV on HIV-associated comorbidities).

Section IV addresses clinically relevant HIV-associated comorbidities. The importance of these comorbidities is reflected by the fact that this section is similar in breadth to both sections I (on clinical manifestations due to primary HIV pathogenesis) and II (on pathophysiological issues). Section IV begins with a contribution on hepatitis C virus (HCV) infection (chapter 21, Radkowski et al.), for which there is mounting evidence of associated neurocognitive impairment that might be synergistic with the neurocognitive effects of HIV itself. Further, these HCV-associated neurocognitive changes do not correlate with the severity of liver disease and are not accounted for by hepatic encephalopathy or by psychoactive substance use disorders, but are indicative, instead, of HCV replication within brain tissue. This chapter is followed by a contribution on CNS toxoplasmosis (chapter 22, Brown and Skiest). Though reduced in incidence, CNS toxoplasmosis remains an important source of morbidity and mortality in the HAART era. The basic and clinical aspects of cytomegalovirus (CMV) infection are then examined (chapter 23, McKendall and Tselis) with regard to CMV encephalitis, polyradiculomyelitis, and mononeuritis multiplex, along with discussion of CMV retinitis. Chapter 24 (Bedimo and Skiest) presents the range of CNS fungal infections, led by cryptococcosis and followed by aspergillosis, coccidioidomycosis, zygomyces, histoplasmosis, blastomycosis, paracoccidioidomycosis, and candidiasis. The appearance of the "great masquerader" is included, with a chapter on neurosyphilis in the setting of HIV infection (chapter 25, Berger and Berger). Of note, the frequency of asymptomatic neurosyphilis is of special concern in the setting of HIV infection. Chapter 26 (Clifford) examines progressive multifocal leukoencephalopathy (PML) in the HAART era. PML patients now have a longer survival time, although proven JC virus-specific therapy for PML remains lacking. Finally, Epstein-Barr virus infection in HIV infection is presented, with a specific focus on primary CNS lymphoma (chapter 27, Tselis and McKendall).

Section IV continues with another unique aspect of this volume, in that this book focuses not only on the neurological conditions associated with HIV infection, but also upon HIV-associated neurobehavioral conditions. Chapter 28 (Ferrando and Loftus) includes sections on depressive disorders, anxiety disorders, delirium, and psychosis. In addition, this chapter focuses on issues experienced by HIV-infected patients that extend into the normal range of neurobehavioral function: fatigue, lipodystrophy syndrome, sleep abnormalities, and sexual dysfunction. There is also a discussion of drug-drug interactions. The last chapter in section IV focuses on psychoactive substance use in HIV infection (chapter 29, Rumbaugh and Nath). Here, basic and clinical sciences are closely interwoven across sections on the opioids, cocaine, methamphetamine, MDMA, alcohol, cannabinoids, and anabolic steroids. Importantly, interactions between prescribed medications and psychoactive substances are discussed.

Yet another uncharacteristic aspect of this volume on neuro-AIDS is represented by its final two sections: section V on special populations, and section VI on special health care issues. Comparatively little can be found in the published literature on these two critical areas. In section V, the special neuro-AIDS populations represented are ethnic groups (chapter 30, Melendez et al.), women (chapter 31,
Arendt et al.), children (chapter 32, Belman), and older persons (chapter 33, Goodkin et al.). Each population is reviewed in detail. In section VI on special health care issues and neuro-AIDS conditions, palliative care issues (chapter 34, Selwyn and Booss), medico-legal issues (chapter 35, Sahai-Srivastava), and international/global issues (chapter 36, Brew) are presented.

In summary, this volume on neuro-AIDS is unique in that it inter-relates data from the pre-HAART and HAART eras across a number of areas covering the domains of pathophysiology, diagnosis, and treatment. The book includes coverage in depth of the disorders due primarily to HIV infection as well as to its associated comorbidities. Likewise, pathophysiological mechanisms of multiple types are delineated. Presentation of the published data on the most relevant neuroimaging techniques for clinical purposes is included. This will aid in bridging the gap between research on disease pathophysiology and clinical practice by promoting the translation of research knowledge in neuroimaging to use in the care for the clinical manifestations of neuro-AIDS. Finally, the book provides coverage of neurobehavioral issues, special population issues, and special health care issues.

In short, The Spectrum of Neuro-AIDS Disorders: Pathophysiology, Diagnosis, and Treatment is a comprehensive volume that we expect to appeal to many readerships, including infectious disease physicians, internists, and other primary care providers; neurologists, neuropsychiatrists, neuropsychologists, neuroradiologists, and neuropathologists; as well as ethnologists, gynecologists, pediatricians, and geriatricians. Likewise, we expect that virologists, immunologists, epidemiologists, biochemists, and pharmacologists can utilize this book. In addition, from the ancillary professions, this book can be appreciated by registered nurses, nurse practitioners, physician assistants, case managers, and medical and psychiatric social workers. Although the ability of these different groups to appreciate various aspects of the text may vary, the attraction of the text to all is its comprehensive delivery of current diagnostic issues and treatment recommendations in neuro-AIDS. Thus, the book holds promise for all of the aforementioned groups.

While the literature in this area advances rapidly, we hope that this volume will retain its appeal over time by its structured approach to the epistemology of neuro-AIDS knowledge. We anticipate that this presentation of the conceptual underpinnings of the neuro-AIDS field will allow new data to continue to be added to the organizational tree of knowledge, resulting in a timeless value for its readers.

I would like to acknowledge the much appreciated contributions of my co-editors, Ashok Verma and Paul Shapshak, who endured the long hours of work required to assemble this volume. In addition, I acknowledge the contribution of Walter G. Bradley, a father of this work who was involved with its original conceptualization. My thanks also go to all of the contributors to this volume and the special efforts they made in submitting each of its chapters, without which the sense of “wholeness” of this volume could not have been achieved. I also thank Jeff Holtmeier, Ken April, Ellie Tupper, Elizabeth McGillicuddy, and the rest of the ASM Press staff who pursued the final goal of publication with both diligence and patience. I wish to thank my loving wife, Amity, and my two sons, Devin and Grant (just approaching his first birthday) for reminding me about everything that is important in life and for allowing me the long hours required to produce this text. Finally, I extend my sincere appreciation to all of the patients and research participants afflicted by neuro-AIDS conditions who have contributed to my work as well as that of all of the authors represented, and without whom this work would not have been possible.

KARL GOODKIN

KARL GOODKIN
Abacavir, 16
for dementia, 513
mitochondrial dysfunction due to, 90, 91
Abscess(es), cerebral
in aspergillosis, 261
in blastomycosis, 356
in candidiasis, 356
diagnosis of, 190
in histoplasmosis, 355
in nocardiosis, 258
in pediatric patients, 461
in toxoplasmosis, 315–316
in tuberculosis, 256–258, 517
Acetaminophen, for fever, 495
Acetylaspartate, in dementia, 249
Acidosis, lactic, see Lactic acidosis
Activities of daily living, with neurocognitive disorders, 34
Acute conversion syndrome, meningitis in, 60–61
Addiction, dopaminergic systems in, 411–412
Adenosylmethionine, for depression, 396–397
Adhesion molecules, in pathogenesis, 138
Adrenal insufficiency, hypotension in, 66
Adult AIDS Clinical Trials Group, on atherosclerosis risk, 52
Advance directives, 494
Advanced HIV infection, complications of, 508–516
Affect, flattened, in pediatric patients, 459–460
African Americans, dementia in, 432–433
Age, see also Elderly persons; Pediatric patients
in cognitive function assessment, 38
in dementia, 433
Aging, see also Elderly persons, HIV infection in brain imaging in, 277
HIV-associated dementia with, 287–288
MRS metabolite peaks in, 287–288
Agitation, palliative treatment of, 495
Agoraphobia, 397
AIDS Clinical Trials Group, on cognitive impairment, 205
AIDS dementia complex, see Dementia, HIV-associated
AIDS dementia complex staging system, 30
AIDS Drug Assistance Program, 501
AIDS Vaccine Integrated Project, 114
Alcohol abuse, 14, 416–417
Alice-in-Wonderland syndrome, in Epstein-Barr virus infections, 386
Alkali therapy, for lactic acidosis, 90–91
Alzheimer's disease
apolipoprotein polymorphisms in, 429
cell cycle proteins in, 236
in HIV infection, 205, 479–480, 509
American Academy of Neurology nomenclature
HIV-associated disorders, 204
neurocognitive disorders, 5, 29–30
Americans with Disabilities Act, 500–501
Anticonvulsants
for distal sensory polyneuropathy, 77–81, 515–516
neuropathy due to, 77–81
Antidepressants
for depression, 394–397
for distal sensory polyneuropathy, 77
for substance abuse, 401
for toxic neuropathies, 80
Antigen(s), cryptococcal, 350
Anti-inflammatory therapies, 18–20
Antioxidants, 21, 219–230
actions of
on blood-brain barrier, 222
in cytokine regulation, 221–223
in oxidative stress, 220–221
for dementia, 141
pro-oxidants and, 222
for psychological well-being, 224–225
recommendations for, 223–224
status of, in HIV, 222–223
for substance abusers, 418
Antiphospholipid antibody syndrome, stroke in, 49
Antipsychotic drugs
delirium, 399–400
neurotoxicity of, 14
for psychosis, 398–399
Antiretroviral drugs, see also specific drugs
classes of, 16–17
combination, see Combination ART drugs of abuse, interactions with, 418
highly active, see HAART
neuropathy due to, 77–81, 515–516
neurotoxicity of, 13–14
for pediatric patients, 463–464
psychotropic drug interactions with, 402–403
Antiretroviral rebound syndrome, 61
Antiviral drug toxic neuropathy, 126
Anxiety, 38, 224–225, 397
Aortitis, in syphilis, 365
Aphasia, in toxoplasmosis, 316
APOBEC3G, inhibitor for, 18
Apoptosis
in dementia, 126–127, 144
drug interactions with, 403
for toxic neuropathies, 80

Downloaded from www.asmscience.org by
IP: 54.70.40.11
On: Sun, 11 Aug 2019 10:05:52
Cytomegalovirus infections, 331–346, 517
clinical manifestations of, 250
neurologic, 335–337
pathophysiology of, 337–339
systemic, 334–335
diagnosis of, 182–183, 186–187
differential diagnosis of, 337
epidemiology of, 334
history of, 331
HIV interactions in, 12, 339
imaging in, 250–252, 336
immune response in, 333–334
interleukins in, 299
latent, 332–333
mononeuropathy multiplex in, 82
pathophysiology of, 250–251
polyneuropathy in, 462
primary, 331–332
progressive polyradiculopathy in, 82
reactivated, 333
recurrent, 333
treatment of, 339–340
vasculopathy in, 48–49, 70
virology of, 331–332
Cytochrome c oxidase, for progressive multifocal leukoencephalopathy, 378

Dana Consortium, dementia studies of, 432
Dapsone
peripheral neuropathy due to, 71, 80
for tocolpasmosis, 322–324
Data Collection on Adverse Effects of Anti-HIV Drugs, 51
dDC, see Zalcitabine (ddC)
dLL, see Didanosine (ddI)
Deep View electrostatic distribution maps, 113
Dehydroepiandrosterone, for depression, 396
Delirium, 399–400
in cytomegalovirus infections, 335
palliative treatment of, 495
Delta-ala1-peptide T-amide, 17
Dementia
cytomegalovirus, 250
HIV-associated, 29, 69–70, 509–514
active, 509
activities of daily living in, 34
aging with, 287–288
alcohol abuse and, 416–417
animal studies of, 288–289
asymptomatic, 276–277
biomarkers for, 430
asymptomatic, 276–277
animal studies of, 288–289
asymptomatic, 276–277
biomarkers for, 430
in elderly persons, 476
encephalitis as etiology of, see
Encephalitis, HIV
epidemiology of, 137, 490, 509
ethnic factors in, 428–434
functional MRI in, 273–280
after HAART introduction, 190–193
HAART effects on, 6–9, 124–129,
137–149, 190–191, 204–206, 219,
250, 286–287, 490
HIV strains and,
430–431
imaging in, 247–250
immunology of, 512
inactive, 509
inflammatory factors in, 10, 12
inflammatory markers in, 287
legal issues in, 501, 503
magnetic resonance spectroscopy in,
281–291
natural history of, 509–510
neuroprotection and, 219–220
oxidative stress in, 219–225
palliative care for, 490–491
pathophysiology of, 8–14, 32–33,
124–129, 137–149, 151–170,
174–176, 204–206, 219–220,
231–238, 247–250, 511–513
presymptomatic detection of, 287
protective strategies for, 128–129
proteomics of, 430
research on, 193–195
screening for, 36–38
severity of, 284–285
subacute progressive, 31
substance abuse with, 411–412
subtypes of, 206
symptoms of, 428
treatment of, 194–195, 238, 513–514
types of, 490
virology of, 8–10, 511–512
in women, 444–445
syphilitic, 367
Demographic factors, in cognitive function assessment, 38
Demelination
in pediatric patients, 460
in progressive multifocal leukoencephalopathy, 375
Deprenyl, for substance abuse, 418
Depression, 32, 38, 394–397
antidepressants for, 224–225
anxiety with, 397
fatigue with, 401
in pain, 401–402
in pediatric patients, 459–460
sleep disorders with, 400
Desipramine
for depression, 395–396
for toxic neuropathies, 80
Developmental problems, in pediatric patients, 459
Dexamethasone
for fatigue, 495
for fever, 495
for nausea and vomiting, 495
Dexamethasin, neuroprotective effects of,
416
Dextroamphetamine, 20
for depression, 396
for fatigue, 495
Diabetes, in autonomic neuropathies, 66
Dichloroacetate, 428
for lactic acidosis, 90
Disease Management Assistance System, 34
Distal sensory polyneuropathy, 70, 75–77,
514–515
pleuritis in, 434–435
gain impairment in, 493
HAART impact on, 126
incidence of, 490
pain management in, 492
in pediatric patients, 462
questionnaire for, 39–101
in women, 445–446
DNA, mitochondrial, inhibitors of, 78–79
DNA polymerases, inhibitors of, 88
Dopamine abnormalities
in dementia, 143–144
substance abuse and, 411–412
Dorsal root degeneration, in syphilis, 364–367
Doxycycline
for neurosyphilis, 370
for tocolpasmosis, 323
Dreams, vivid, 400
Driving, automobile, 34–36, 503
Dronabinol
for nausea and vomiting, 495
neurologic effects of, 416
for weight loss, 495
Drug(s)
abuse of, 418
substance abuse neuropathies due to, 70–71
patient management of, neurocognitive disorders and
peripheral neuropathies due to, 70–71,
76–81
DSP, see Distal sensory polyneuropathy
d4T, see Stavudine (d4T)
Durable power of attorney, for dementia
patients, 491
Durban Stroke Data Bank, 46–47
Duty to warn third parties, about HIV test results, 500
Dying, palliative care in, 494–496
Dynamic susceptibility contrast, in perfusion MRI, 273–274
Dysautonomia, see Autonomic neuropathy(ies)
Dysesthesias, in distal sensory polyneuropathy, 75
Dyslipidemia, 13
stroke in, 51–52
treatment of, 21
Dyspnea
in lactic acidosis, 90
palliative treatment of, 495
Ear, syphilis of, 368, 371
Ear, syphilis of, 368, 371
Early antigen, in Epstein-Barr virus infections, 387

Dipteral-type syndrome, in pediatric patients, 459
Diaphragm, for neurosyphilis, 370
for tocolpasmosis, 323

Diving, automobile, 34–36, 503

Dronabinol
for nausea and vomiting, 495
neurologic effects of, 416
for weight loss, 495

Drug(s)
abuse of, 418
substance abuse neuropathies due to, 70–71
patient management of, neurocognitive disorders and
peripheral neuropathies due to, 70–71,
76–81
DSP, see Distal sensory polyneuropathy
d4T, see Stavudine (d4T)
Durable power of attorney, for dementia
patients, 491
Durban Stroke Data Bank, 46–47
Duty to warn third parties, about HIV test results, 500
Dying, palliative care in, 494–496
Dynamic susceptibility contrast, in perfusion MRI, 273–274
Dysautonomia, see Autonomic neuropathy(ies)
Dysesthesias, in distal sensory polyneuropathy, 75
Dyslipidemia, 13
stroke in, 51–52
treatment of, 21
Dyspnea
in lactic acidosis, 90
palliative treatment of, 495

Ear, syphilis of, 368, 371

Early antigen, in Epstein-Barr virus infections, 387

Dipteral-type syndrome, in pediatric patients, 459
Diaphragm, for neurosyphilis, 370
for tocolpasmosis, 323

Diving, automobile, 34–36, 503

Dronabinol
for nausea and vomiting, 495
neurologic effects of, 416
for weight loss, 495

Drug(s)
abuse of, 418
substance abuse neuropathies due to, 70–71
patient management of, neurocognitive disorders and
peripheral neuropathies due to, 70–71,
76–81
DSP, see Distal sensory polyneuropathy
d4T, see Stavudine (d4T)
Durable power of attorney, for dementia
patients, 491
Durban Stroke Data Bank, 46–47
Duty to warn third parties, about HIV test results, 500
Dying, palliative care in, 494–496
Dynamic susceptibility contrast, in perfusion MRI, 273–274
Dysautonomia, see Autonomic neuropathy(ies)
Dysesthesias, in distal sensory polyneuropathy, 75
Dyslipidemia, 13
stroke in, 51–52
treatment of, 21
Dyspnea
in lactic acidosis, 90
palliative treatment of, 495

Ear, syphilis of, 368, 371

Early antigen, in Epstein-Barr virus infections, 387
INDEX
INDEX

Neurosyphilis (continued)
clinical manifestations of, 364–368
complications of, 370
diagnosis of, 369–370
epidemiology of, 364
etiology of, 363
historical background of, 363
HIV interactions in, 13
in progressive polyradiculopathy, 82
in toxoplasmic encephalitis, 313–315
NPZ approach, to cognitive function
Northeast AIDS Dementia test battery,
Nonnucleoside reverse transcriptase inhibitors
Nonbacterial thrombotic endocarditis,
Nocardiosis
Nitric oxide, in dementia, 512
Nissl-Alzheimer arteritis, 255, 364
New Delhi Declaration, 505
Nevirapine, 17
Neurotrophic factors, cell cycle protein
Neurotransmitter modulators, 20–21
meningovascular, 366, 368, 370–371
modified, 368
natural history of, with HIV infection, 368
parenchymatous, 364
pathophysiology of, 255, 364
prognosis for, 370
risk factors for, 364
treatment of, 370–371
vasculopathy in, 48
Neurotoxins
in dementia, 139–145
in encephalitis, 231
in HAND, 153
Neuronal marker modulators, 20–21
Neurotrophic factors, cell cycle protein interactions with, 235–236
Nevirapine, 17
for dementia, 514
psychotropic drug interactions with, 402
New Delhi Declaration, 505
Nimodipine, 18, 145
Nissl-Alzheimer arteritis, 255, 364
Nitric oxide, in dementia, 512
NMDA receptor antagonists, for dementia protection, 128–129
Nocardiosis
diagnosis of, 190
imaging in, 258
pathophysiology of, 258
Nonbacterial thrombotic endocarditis, stroke in, 47–48
Nonnucleoside reverse transcriptase inhibitors, 16–17
for dementia, 513–514
dual regimen of, 6
mechanism of action of, 4–5
psychotropic drug interactions with, 402–403
Nontreponemal tests, in neurosyphilis, 368–370
Northeast AIDS Dementia test battery, 37
Northeastern AIDS Dementia cohort, ethnic studies of, 432
NPZ approach, to cognitive function assessment, 38
Nucleoside neuropathy, 515–516
Nucleoside reverse transcriptase inhibitors for dementia, 513–514
mechanism of action of, 4–5
mitochondrial dysfunction due to, 87–92
psychotropic drug interactions with, 402–403
Nummness, in distal sensory polyneuropathy, 75
Nursing homes, 494
Nutrition, 21
inadequate, oxidative stress and, 222–223
in palliative care, 494–495
Occupational Safety and Health Administration, infection prevention regulations of, 503
Ocular disorders, see Eye
Olanzapine, 21
delirium, 399–400
for mania, 398
Oligodendrocytes, JC virus in, 375–376
Onadurseron, for nausea and vomiting, 496
Oxycystis, Toxoplasma gondii, 313–315
OPC-14117 antioxidant, for dementia protection, 145
Opiate cofactor hypothesis, 413
Opioids, abuse of, 412–414
Opportunistic infections, see also specific infections vs. dementia, 174
HIV interactions in, 12–13
imaging of, 250–265
incidence of, HAART and, 184
in pediatric patients, 461
vasculopathy in, 48–49
Optic atrophy, in syphilis, 368
Oral leukoplakia, in Epstein-Barr virus strain identifications, 202
for Epstein-Barr virus infections, 386
Orthostatic hypotension, 65–66, 71
Outcomes, surrogate markers for, 95–103
“Owl’s eye” appearance, of cytomegalovirus, 331
Oxandrolone, for weight loss, 495
Oxazepam, for anxiety, 397
Oxidative phosphorylation, in mitochondria, 87
Oxidative stress, 219–230
antioxidant protection against, 220–221, 223–224
in cocaine abuse, 414
in dementia, 141–142, 512
in methamphetamine abuse, 415
pathologic effects of, 219–220
Oxytocin deficiency, 70
p53 protein
in Alzheimer’s disease, 236
in cellular viability regulation, 232–233
in encephalitis, 235–238
Pain, 401–402
in distal sensory polyneuropathy, 515
management of
in palliative care, 491–493
in pediatric patients, 464
in toxic neuropathies, 80
neuropathic, 70, 491–493
Palliative care, 489–497
conditions requiring, 490–493
at end of life, 494–496
mortality trends and, 489–490
services for, 493–494
Panic disorder, 397
Pantothenic acid, antioxidant action of, 232–233
Paracoccidioidomycosis, 356
Paralysis
in dementia, 509
in myelopathy, 57
in progressive polyradiculopathy, 82
Parasitic infections, imaging in, 261–265
Paraventricular nucleus, dysfunction of, 70
Paresis, in syphilis, 364, 367
Paresthesias
in distal sensory polyneuropathy, 75, 515
in progressive polyradiculopathy, 82
Parkinson’s disease, cell cycle proteins in, 236
Parkinson’s disease symptoms in dementia, 3, 143–144
in substance abuse, 411–412
Paroxetine, for depression, 395
Pathophysiology of aspergillosis, 60
of autonomic neuropathy, 69–71
cryptococcosis, 259–260, 348–349
cytomegalovirus infections, 250–251, 337–339
dementia, 511–513
antioxidants in, 219–224
cell cycle proteins and, 231–238
cerebrospinal fluid markers for, 173–176
chemokines in, 124, 138, 140–141, 151–170
HAART effects on, 124–129, 204–206
imaging in, 247–250
viral genetic variability in, 201–211
distal sensory polyneuropathy, 514–515
doctor-induced mitochondrial dysfunction, 87–90
of encephalitis, 137–149, 204–206
cell cycle proteins and, 231–238
of encephalopathy, 181–193
of Epstein-Barr virus infections, 385
factors contributing to, 8–14
comorbid infections, 12–13
infectious, 10–12
inflammatory, 13–14
vascular, 13
virologic, 8–10
HAART effects on, 124–129
of HAND, chemokines in, 151–160
of herpes simplex virus infections, 254–255
of lymphoma, 265–267
of myelopathy, 47–49
of myopathy, 60
of neurocognitive disorders, 32–33
of neurosyphilis, 255, 364
of nocardiosis, 258
of opioid abuse, 412–413
in pediatric patients, 460–461
of peripheral neuropathy, 75–82
of primary CNS lymphoma, 387–388
of progressive multifocal leukoencephalopathy, 252–253, 375–376
of stroke, 47–52
of syphilis, 255, 364
of toxic neuropathy, 515–516
of toxoplasmosis, 262–265, 313–315
of tuberculosis, 256–258
of variella-zoster virus infections, 255
Paul-Bunnell test, 383
PCR
for cytomegalovirus, 251, 336–337
for Epstein-Barr virus, 387
for strain identification, 202
for Toxoplasma, 318–319
Pediatric patients
HIV infection in, 455–457
cerebrovascular complications in, 461–462
encephalopathy in, 458–459, 464
HIV-related vasculopathy, 50–51
immune vasculopathy, 48–49
in pediatric patients, 461–462
Stromal-cell-derived factor 1 alpha, in neurocognitive pathophysiology, 10, 11
Substance abuse, 400–401
alcohol, 14, 416–417
anabolic steroids, 417
cannabinoids, 417
cocaine, 14, 414
in dementia pathogenesis, 14
dopaminergic action in, 411–412
intravenous, HIV transmission in, 457
legal issues in, 504
methylamphetamine, 14, 414–415
opioids, 412–414
pain management in, 491
peripheral neuropathies due to, 417
promoting genetic variability, 203
Sulfadiazine, for toxoplasmosis, 321–323
Sulfadiazine, for toxoplasmosis, 324
Sulfonaphane, antioxidant action of, 221
Superoxide dismutase, in dementia, 141–142
Superoxide dismutase, antioxidant action of, 221
in dementia, 220
Suppressors of cytokine signaling proteins, 368–370
Surface-enhanced laser desorption ionization time of flight, in proteomics, of dementia, 430
Surrogate markers, for clinical outcomes, 95–103
case-cohort studies, 98–101
definition of, 95–96
operational criteria for, 95–96
statistical validation of, 96–98
survival, 98–99
Sweats, palliative treatment of, 495
Syringe exchange programs, 504
T20 (fuzone), for dementia, 514
T lymphocytes
apoptosis of, 126–127
CD4
vs. autonomic neuropathy, 68
cognitive function, 32
viral genetic variability and, 211
CD8
vaccine development and, 108–109
viral genetic variability and, 210–211
in cytomegalovirus response, 333–334
cytotoxic, in neurocognitive pathophysiology, 12
Epstein-Barr virus in, 384, 385, 388
regulatory, depletion of, 109–110
vaccine development and, 107–115
Tabes dorsalis, 364–367
Tachycardia, 67
in autonomic neuropathies, 66
in lact acidosis, 90
Tachypnea, in lact acidosis, 90
Tachyzoites, Toxoplasma gondii, 312
Tat protein
alcohol interactions with, 417
coenzyme interactions with, 414
in dementia, 10, 140–144, 220, 509, 512
in HAND, chemokines and, 152–153
methylamphetamine interactions with, 415
opioid interactions with, 413–414
in vaccine development, 18
Tattooing, regulation of, 504–505
Temazepam, for anxiety, 397
Testing
tolerability, in immunity, 107
Tolerance, in immunity, 107
Tocopherol, antioxidant action of, 221, 224
Tkip protein, as vaccine target, 109
Tissue plasminogen activator, for treatment of, 80–81
Titer, in vaccine development, 18
Tissue culture, Toxoplasma gondii, 318
Tissue plasminogen activator, for treatment of, 80–81
Tissue, Toxoplasma gondii, 318
Tocopherol, antioxidant action of, 221, 224
Tolerance, in immunity, 107
Topotecan, for progressive multifocal leukoencephalopathy, 378
Torsades de pointes, in autonomic neuropathies, 66, 68
Toxic neuropathies, 76–81
antiretroviral, 515–516
antiviral agents, 126
dapsone, 71, 80
didanosine, 78
in elderly persons, 482
ethambutol, 80
isoniazid, 79
mechanisms of, 78–79
metronidazole, 80
in pediatric patients, 462, 464
pyridoxine, 79–80
stavudine, 78
thalidomide, 79
treatment of, 80–81
vincristine, 70–71, 80
in women, 445–446
Toxoplasmosis, 313–329, 337–341
clinical manifestations of, 316–317
diagnosis of, 183, 187, 317–321
epidemiology of, 313
imaging in, 261–265, 319–320
immune response in, 315
ocul, 317
organism life cycle in, 313–315
pathophysiology of, 262–265, 313–315
prophylaxis for, 323–324
risk factors for, 317
treatment of, 321–323
vasculopathy in, 48–49, 70
Transcutaneous protein, see Tat protein
Transfusions, HIV transmission in, 457
Transient ischemic attack
in elderly persons, 481
in pediatric patients, 461–462
Transplantation, cytomegalovirus infections in, 333, 335
Transverse myelitis
HIV, 507
syphilitic, 367
Trazodone, for anxiety, 397
Treatment, 16–22; see also Antiretroviral drugs; Vaccines; specific drugs and disorders
anti-inflammatory, 18–20
ethical issues in, 503
immune, 18–20
legal issues in, 501, 503
neurotransmitter modulators in, 22–21
nutritional, 21
palliative, 495
potential agents for, 21–22
refusal of treatment, 501, 503
Treponema pallidum infections, see Neurosyphilis; Syphilis
Treponemal pallidum hemagglutination test, 369
Treponemal tests, in neurosyphilis, 368–370
Tricyclic antidepressants, for depression, 395
Triglycerides, elevated, stroke in, 51–52
Trimethoprim-sulfamethoxazole
autonomic neuropathy due to, 71
for toxoplasmosis, 322–324
Trimodulatex, for toxoplasmosis, 322
Trk receptors, in HAND, 154
“Trojan horse” phenomenon in hepatitis C, 303–304
in HIV infection, 124
Tropism, cellular, of HIV, 9
Trypanosoma cruzi infections, 190
Tuberculomas, 256–257, 517
Tuberculosis, 517
diagnosis of, 189
HIV interactions in, 12–13
imaging in, 256–258
pathophysiology of, 256–258
stroke in, 516
vasculopathy in, 48
Tumor necrosis factor-α
antioxidant effects on, 221–222
in cytomegalovirus reactivation, 333
in dementia, 140, 144, 220, 512
in HAND, 153
inhibitors of, 19
in neurocognitive pathophysiology, 10, 11
polymorphisms in, dementia and, 429
in vaccine development, 18
in vasculopathy, 49
Ulceration, in primary HIV infection, 507
United Nations General Assembly, HIV declarations of, 505
Uveitis, in toxoplasmosis, 317
Vaccines, 18
antigens for cell-mediated immunity recognition of, 107–115
selection of, 107
Vaccines
  genetic variability problems with, 210–211
gp120 peptide, 110–115
history of, 105–106
HIV evolution and, 109
HLA supertypes and, 106–107
mucosal, 109
Vaccinaric acid, 367
Vacuolar leukoencephalopathy, 511
Vacuolar myelopathy, 57–59, 70, 493
in dementia, 511–513
diagnosis of, 190
Vagus nerve dysfunction, 67
Valganciclovir, for cytomegalovirus infections, 339–340
Valproate, 20
  for dementia protection, 128, 145
  for distal sensory polyneuropathy, 515
  for mania, 397–398
Varicella-zoster virus infections
  imaging in, 255
  pathophysiology of, 255
  stroke in, 515
vasculopathy in, 49
Vasculitis
  in pediatric patients, 462
  in HIV-related, 50–51
  in immune disorders, 48–49
  in opportunistic infections, 48–49
VCA antigen, in Epstein-Barr virus infections, 387
VDRL, 368–371
Venlafaxine, for depression, 396
Ventriculitis, nocardial, 352
Ventriculitis, for cytomegalovirus infections, 339–340
Virology
  cytomegalovirus, 331–334
  Epstein-Barr virus, 383–384
  HIV
    in dementia, 511–512
    drug actions and, 4–5
    pathophysiology and, 8–10
    strains, see Strains, HIV
    structure, 4–5
  viral RNA, 175
Visual loss
  in cryptococcosis, 349
  in progressive multifocal leukoencephalopathy, 376
  in toxoplasmosis, 316
Vitamin(s)
  antioxidant action of, 221–223
  deficiency of, 222–223
  supplementation of, 21, 91
Vitamin B group, antioxidant actions of, 225
  Vitamin B12
    antioxidant action of, 221
    deficiency of, myelopathy in, 58, 59
  Vitamin C, antioxidant action of, 221
  Vitamin E, antioxidant action of, 221
Vocational functioning, see Employment
Vomiting
  in autonomic neuropathy, 66
Voriconazole
  for aspergillosis, 354–355
  for cryptococcosis, 352
Wasting syndrome, 502
Weakness
  in myelopathy, 57, 58
  in myopathy, 59–60
  palliative treatment of, 495
  Western blot test, for strain identification, 202
White-matter lesions
  in cytomegalovirus infections, 250–252
  in dementia, 248, 511
  in hepatitis C, 301
  imaging in, 248
  in progressive multifocal leukoencephalopathy, 252–253, 376–377
Women, HIV infection in, 443–454
  asymptomatic neuropsychological impairment in, 444–445
dementia in, 433–434, 444–445
distal sensory polyneuropathy in, 445–446
German cohort of, 446–448
HIV statistics for, 443–444
inequality of, promoting genetic variability, 203
migration and, 448–450
minor cognitive-motor disorder in, 444–445
neuro-AIDS in, 446–448
neuropsychiatric disorders in, 448
sensory neuropathies in, 445–446
testing of, 443
therapy response in, 444
toxic neuropathies in, 445–446
Work performance, see Employment
  Working memory, in elderly persons, 477
World Health Organization
  analgesic ladder of, 80, 492
  palliative care definition of, 489
Zalcitabine (ddC), 16
  mitochondrial dysfunction due to, 90
  neuropathy due to, 71, 77–78, 515–516
Zidovudine, 16
  mitochondrial dysfunction due to, 90
  neuropathy due to, 71
  disease recrudescence with, 5
  for encephalopathy, 464
  mitochondrial dysfunction due to, 90
  myopathy due to, 60
  for primary HIV infection, 508
Zinc
  antioxidant action of, 221–224
  deficiency of, 223
Zonisamide, 21, 399–400
Ziprasidone, 21, 399–400
Zygomycosis, 355