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Book Review Editor

Mitochondrial Inhibitors and Neurodegenerative Disorders

Edited by Paul R. Sanberg, Hitoo Nishino, and Cesario V. Borlongan
Totowa, NJ, Humana Press, 2000, 313 pages, ISBN 0–896–03805-X, $125.00

Reviewed by William S. Musser, M.D.

The mitochondrion is an important constituent of the eukaryotic cell. Its inner membrane is the site of cellular respiration, which provides the cell with adenosine triphosphate (ATP) via the Krebs cycle and the electron transport chain. When mitochondrial dysfunction occurs, the effects may be widespread, affecting the central and peripheral nervous system, the visual system, the auditory system, and muscle. The discovery of toxins, both natural and synthetic, that disrupt mitochondrial function has allowed for the development of experimental models of mitochondrial disease. *Mitochondrial Inhibitors and Neurodegenerative Disorders* details one such toxin, 3-nitropropionic acid (3-NPA), an irreversible inhibitor of succinate dehydrogenase, and its use in experimental models of central nervous system neurotoxicity and neurodegenerative diseases like Huntington's disease (HD).

This is a multi-authored text. Most of its contributors are basic researchers in the area of mitochondrial function, as are its three editors. The book contains 20 chapters divided among three subject areas: mitochondrial toxins, models of neurodegeneration secondary to mitochondrial dysfunction, and treatment strategies for mitochondrial-induced neurotoxicity.

The opening chapter, by Mohammad I. Sabri, Peter S. Spencer, Safia Baagia, and Albert C. Ludolph, provides an overview of both the clinical symptomatology and the mechanisms of actions of several mitochondrial toxins, including 3-NPA, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), and cyanide. The second chapter, by Bradley F. Hamilton, Daniel H. Gould, and David L. Gustine, focuses on the clinical manifestations of 3-NPA intoxication in both animals and humans, while the third chapter, by Norman C. Reynolds and Wen Lin, details the biochemistry and neurochemistry of 3-NPA.

Animal intoxication with 3-NPA usually occurs when livestock in the western United States or Canada ingest a member of the *Astragalus* species of plant. Intoxication may be either acute or chronic. In the acute form in cattle, generalized weakness and incoordination develop, which may progress to respiratory distress, coma, and death, depending on the amount of toxin ingested. The chronic form in cattle consists of both respiratory dysfunction and incoordination.

Outbreaks of 3-NPA toxicity in humans have been described in China. Generalized and neurologic symptoms have been reported in children after they ingested moldy sugarcane contaminated with the fungal species *Arthrinium*. A spectrum of clinical manifestations develops within a few hours of ingestion of moldy sugarcane, varying from gastrointestinal symptoms and headache to coma, seizures, and death. For those who survive the initial manifestations, dystonia will develop in up to one-half within 7 to 40 days after ingestion. The dystonia tends to be persistent and nonprogressive. CT scans of those affected demonstrate hypodense lesions in the basal ganglia.

The second section of the book describes animal models of 3-NPA–induced neurodegeneration. Each chapter in this section opens with a brief introduction and statement of the authors' particular hypotheses (including models of cognitive dysfunction, gender-based differences in neurotoxicity, and a model of neuronal death in HD), followed by a presentation of the authors' own data and their conclusions. Although this section is clearly and uniformly written, one wonders how a peer reviewer would respond to the experimental methodology, the data, and the conclusions as they are currently presented. This section does point out that the striatum appears to be selectively vulnerable to the affects of 3-NPA but that it is unclear whether the mechanism of such vulnerability is excitotoxicity, apoptosis, or oxidative stress.

The final section of the book discusses experimental mechanisms for prevention of mitochondrial toxin–induced neurotoxicity. The first chapter, "Neuroprotective Strategies Against Cellular Hypoxia," by Matthias W. Riepe, both describes the basic mechanisms of hypoxic damage to neurons and reviews the agents-to-date that have been used in studies of neuroprotection. The theme of this chapter, that 3-NPA-induced chemical hypoxia may be used as a neuroprotective strategy, is then pre-

sented and possible mechanisms are discussed. The three remaining chapters are similarly organized. Data concerning the protective effect of perinatal ischemic-hypoxic injury on subsequent 3-NPA neurotoxicity in rats, the therapeutic effect of fetal transplant into rat striatum to reverse 3-NPA–induced akinesia, and other therapeutic strategies to combat MPTP and 3-NPA neurodegeneration are reviewed and the results discussed.

The majority of the black-and-white figures in the book, while simple, clearly illustrate the authors' points. Some, however, appear to be personal computer–generated presentation slides that the authors simply pasted into the text. Tables and graphs, also presented in a black-and-white format, adequately illustrate the data on which the authors base their conclusions.

This is a technically oriented book whose main audience will be basic researchers with a specific interest in both mitochondrial function and the use of mitochondrial toxins as a method of creating animal models of neurodegeneration. Although the authors speculate on the use of such models to delineate the pathologic mechanisms of Alzheimer's disease, Parkinson's disease, and Huntington's disease, this speculation appears a bit premature; further work will be necessary to delineate the pathophysiologic mechanisms responsible for these disorders. This is not a book for the practicing neuropsychiatrist, since the experimental methodologies described are works in progress and as yet have limited clinical relevance. Instead, *Mitochondrial Inhibitors and Neurodegenerative Disorders* is a concise summary of the present state of research in the area of mitochondrial toxins and their role in animal models of neurodegenerative disease.

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Diagnosis and Management of Dementia: A Manual for Memory Disorders Teams

Edited by Gordon K. Wilcock, Romala S. Bucks, and Kenneth Rockwood

New York, Oxford University Press, 1999, 416 pages, ISBN 0-19-262815-1 (cloth), 0-19-262822-4 (paper), $39.95

Reviewed by Gayatri Devi, M.D.

This is a well thought out, well edited, comprehensive overview of all aspects of establishing and running a memory disorders center. The contributors are primarily from the United Kingdom, with additional chapters from experts in Australia, Canada, and the United States.

The first section of the book takes a hands-on approach to the details of establishing and organizing a dementia clinic—including ideal location, physical plant layout, database setup, consideration of referral sources, and the composition of an effective memory evaluation team. The minutiae of recordkeeping as it pertains to memory disorders are succinctly dealt with. Ideal formats for the diagnostic visit and the informing visit, where the diagnosis is conveyed to families, are discussed. Patient follow-up is recommended at 6 months after the first visit, then at 12 months, then at 24 months. Thereafter, annual telephone contact is suggested. (This frequency of follow-up is probably less than the reviewer would be comfortable with.)

The medical, psychiatric, and laboratory investigations needed to arrive at a diagnosis are reviewed, as well as the use of neuropsychological and computerized cognitive batteries. A comparison of standardized neuropsychological tests from samples sited in the United Kingdom and the United States is illuminating, revealing more of a skew toward American tests such as the Wechsler Memory Scale in the United States. Computerized batteries are rightly felt to be adjunctive tools and not adequate substitutes for traditional test administration.

The role of speech and language therapy in patients with dementia is addressed through representative cases. The functional assessment, utility of home visits, and methods of using memory disorders clinics for research are discussed and illustrated with case studies.

The book's second section defines and discusses age-related cognitive decline, Alzheimer's, and other dementias. The third section deals with management. These two sections, however, are brief compared with the earlier detailed section. Pharmacological and behavioral interventions, cognitive therapy, and caregiver management are described, and there is a useful list of the Internet addresses of websites that serve as sources of information for memory disorders.

A fascinating final chapter, authored by the editors, examines the composition and current practices of 28 memory disorder clinics represented by the contributing authors to the book. The specialist makeup, tests administered, referrals arranged, and other details are described, giving a glimpse into the standard working practices of an array of memory clinics worldwide.

This book covers, from the ground up, most foreseeable issues involved in the implementation and management of a memory disorders

clinic and would prove useful not only to persons involved in establishing a memory disorders center, but also to those who are interested in expanding currently offered services at their offices. The merging of British and American viewpoints in the evaluation and management of dementia is refreshing and informative.

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Attention Deficits and Hyperactivity in Children and Adults, 2nd edition, revised and expanded

Edited by Pasquale J. Accardo, Thomas A. Blondis, Barbara Y. Whitman, and Mark A. Stein
New York, Marcel Dekker, 2000, ISBN 0-8247-1962-X, $85.00

Reviewed by Barbara Z. Novick, Ph.D.

Attention-deficit/hyperactivity disorder (ADHD) has certainly been the "diagnosis of the decade." Very young children and preschoolers, as well as school-age children and adults, receive the diagnosis today in record numbers. This occurs even though enormous concern remains about the lack of standard assessment and management procedures and about misdiagnosis and inadequate treatment protocols. ADHD has received a great deal of attention in the lay press and in the professional press; still, I for one am grateful to the editors of this book for their decision to add an important and unique volume to the overcrowded field of ADHD literature. Its predecessor, *Attention Deficit Disorder and Hyperactivity in Children: Early Diagnosis and Intervention*, was published nearly a decade ago. Its goal was to provide an interdisciplinary and medically focused text devoted to the field of ADHD. The new edition has the same focus, but it is both more comprehensive and more detailed than its predecessor. At the same time, it is more accessible to laypersons and also more of an aid to clinicians who need to communicate the complexities of ADHD to adults who may be concerned primarily about themselves, their children, or both.

The volume begins with a historical introduction to ADHD and a discussion of the physiological substrate. Next is a detailed discussion of clinical diagnosis. This includes an overview focused on neurodevelopmental and psychoeducational assessment of children suspected of having ADHD; methods of measuring attention deficits with and without hyperactivity; gender issues and ADHD; and adaptive function in children with ADHD. A discussion of comorbidity and ADHD in clinical diagnosis includes a look at developmental learning and language disorders, developmental coordination disorders, disruptive behavior disorders, and mood symptoms in children with ADHD. Finally, the discussion of clinical diagnosis focuses on associated deficit conditions that mimic ADHD and alternative etiologies; these include plumbism, alcohol exposure in utero, fragile X syndrome, Tourette's syndrome, pervasive developmental disorder spectrum, thyroid dysfunction, and hearing loss. The section devoted to therapy for individuals with ADHD discusses strategies for living with a child with the disorder and for managing that child in school, pharmacologic management, social skill enhancement in children with ADHD, adjunctive therapies, and multidisciplinary approaches. The final section of the volume discusses a number of important other issues, such as benefits of early identification and treatment, legal issues, and adult outcomes for individuals with ADHD.

In all, this very impressive work provides coverage of the newest and most exciting basic science information about underlying diagnosis, therapy and biological substrates, outcomes, and many other fascinating and challenging issues (including legal issues) vis-à-vis ADHD. Moreover, a section at the end of each chapter, called "Points for Parents," provides a summary of the contents of each chapter in language that is entirely intelligible to nonprofessionals. This book should be invaluable not only to professionals concerned about ADHD, but also to countless other adults who both need and seek an up-to-date overview of this exciting and complex topic.

Dr. Novick is director of the Center of Attention and Learning Disorders, Lenox Hill Hospital, New York, NY.