Book Reviews

EPILEPSY: MODELS, MECHANISMS AND CONCEPTS. 1993. Edited by Philip A. Schwartzkroin. Published by Cambridge University Press. 544 pages. $CDN 162.00.

Understanding the basic mechanisms of epilepsy presents a formidable scientific challenge. Epilepsy is not a disease but rather an umbrella term covering a multi-dimensional group of disorders associated with a wide variety of pathologies and biochemical disturbances that share the tendency to recurrent seizures. Both technical and conceptual limitations severely constrain direct investigation of basic mechanisms in patients. Investigators have, therefore, turned to animal models to study the pathophysiology of epilepsy. So many different models have been developed that there may now be more models than patients. This book is fortunately not a comprehensive survey of available epilepsy models. Instead, it focuses on a limited number of well-studied models to identify important conceptual frameworks that have emerged from their investigation.

The book is organized into three sections of five chapters. Each chapter, written by recognized authorities, describes a particular model and attempts to identify major concepts that have arisen from studying it or the types of issues which it is most suitable for investigating. The first section describes chronic models in intact animals and introduces some of the key issues. The kindling model, a variety of genetic animal models and the susceptibility of the immature brain to seizures are used to examine factors responsible for the development of the seizure-prone state or epileptogenesis. Intact animal models are also used to develop the idea that certain brain regions, particularly in the limbic system, act as epileptic "trigger" zones which either initiate seizures or serve as critical relays in the propagation of seizures. These models provide important links between simplified experimental preparations and the human epilepsies.

The second and third sections describe mainly *in vitro* models that have been used to study epileptic tissue and normal brain mechanisms that support epileptiform activity. The technical advantages provided by preparations such as the hippocampal and neocortical slice have been exploited to examine the cellular mechanisms underlying hyperexcitablity and hypersynchrony in the immature brain and in 'normal' brain rendered 'epileptic' by a variety of convulsant stimuli. These studies have yielded a rich array of hypotheses concerning the complex interplay among voltage- and ligand-gated ion channels embedded within recurrent excitatory and inhibitory local circuits that can account for the pacemaker properties of epileptic 'trigger' zones such as the hippocampal CA3 region. Studies on kindling and a model of limbic status epilepticus have identified the dentate gyrus as a critical 'gate' which normally prevents excessive activation of the hippocampus proper. One of the most important ideas that has emerged from epilepsy research is that seizures may render the brain permanently hyperexcitable. Several excellent chapters in section 2 discuss some of the mechanisms responsible for neuronal plasticity in response to seizures and neuronal damage as well as their potential relationship to epileptogenesis. However, the chapter describing *in vitro* studies on tissue removed from patients undergoing surgery for intractable epilepsy indicates that the hypotheses generated from the experimental models have yet to be confirmed in the 'human model'. Perhaps more subtle experimental models are needed.

Although it is not intended to be comprehensive, this book covers a broad spectrum of important issues and concepts and should stimulate discussion among clinical epileptologists and basic scientists interested in the pathophysiology of epilepsy. Most of the chapters are well written and adhere to the goal of describing key observations which have lead to important hypotheses. It is entirely fitting that the chapter by Jo-Ann Frank (in whose memory the book is dedicated) on the use of models of hippocampal sclerosis to investigate the relationships between seizures, neuronal plasticity and cell death is perhaps the best example of how critical appraisal of well-studied animal models can provide important insights into complex problems.

A few of the chapters in the first section present too much experimental detail. This sometimes obscures the concepts and makes for difficulty reading. However, this problem is largely offset by Dr. Schwartzkroin's introductions to each section. These, along with the general introduction to the book, highlight and amplify the major hypotheses discussed in each chapter and place them in a broader context. The introductory chapters, read on their own, provide a lucid, well thought out review of many of the major issues in epilepsy research and much of the progress that has been made over the past few decades. I highly recommend this volume.

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STROKE: PATHOPHYSIOLOGY, DIAGNOSIS AND MANAGEMENT. 2nd Edition, 1992. By Henry J.M. Barnett, J.P. Mohr, Bennett M. Stein and Frank M. Yatsu. Published by Churchill Livingstone, New York, Edinburgh, London, Melbourne and Tokyo. 1270 pages. $CDN 304.00

The second edition of "Stroke: Pathophysiology, Diagnosis and Management" is a comprehensive and up-to-date reference on cerebrovascular diseases. It is a multi-authored text conveniently divided into five sections.

The "Pathophysiology" section begins with a detailed overview of the epidemiology and risk factors for stroke. Dr. P.A. Wolf et al. provide useful information on hypertension, smoking, cholesterol, atrial fibrillation and other risk factors for stroke. Subsequent chapters on atherosclerosis, animal models of stroke, neurochemistry of stroke and PET studies in stroke are meant for neurologists with a special interest in stroke. The final section on pathology of stroke by Garcia et al. provides good illustrations on sub-types of stroke. It is a useful text for physicians interested in understanding mechanisms of cerebrovascular disease.

The section on "Diagnostic Studies for Stroke" provides practical guidelines to all physicians who see stroke patients on a regular basis. Dr. Mohr provides a concise overview of the available tests, their current indications and limitations in various stroke sub-types. This is followed by comprehensive and detailed reviews on the use of CT, MRI, cerebral angiography and ultrasound in cerebrovascular disease. There are excellent illustrations in each section which do not lose there quality in the printing process.

The section on the "Clinical Manifestations of Stroke" begins with a overview of the classification of stroke. This is followed by detailed discussions on the clinical presentation of stroke in the various cerebral arteries. Whereas the overview is useful and easy to read, subsequent chapters on arterial syndromes contain details on localization that are somewhat redundant for this text. The section on "Specific Medical Disease and Stroke" is a valuable reference source on uncommon stroke-subtypes.

The final section "Stroke Therapy" is perhaps the most practical section for the general neurologist. There are firm guidelines on the use of antiplatelet and anticoagulant medications and surgery in secondary prevention of stroke.

Stroke is the third most common cause of death in North America. It remains the most neglected chronic neurological disorder. In the last decade there have been significant gains in understanding epidemiology of risk factors, mechanisms, investigations and treatment of acute stroke. The next five years will witness increasing trials of neuroprotective agents and thrombolysis after acute stroke. An increased awareness of the problem and rapid evaluation of patients will be essential for successful completion of these trials. This text does an excellent job of reviewing the accepted rational therapy in cerebrovascular diseases. It also identifies areas where further research is urgently needed to further improve outcomes in patients at risk for stroke.

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PARKINSON'S DISEASE – SYMPOSIUM REVIEW (1992). 1993. Edited by Merton Sadler. Published by John Libbey, London, Paris, Rome. 65 pages.

The book consists of four chapters written by J. Jankovic, E. Tolosa, W. Olanow, and M. Sandler based on papers presented at a Symposium in Maastricht, Germany in 1992.

The first chapter on strategies for treatment reviews the major theories on production of substantia nigra damage. The table on classification of parkinsonism is very good as is the table dealing with medical and surgical management. The authors outline the drugs currently available as well as those under investigation. There are many valuable pearls on management of Parkinson's disease by an experienced clinician. The tables on fluctuations and dyskinesias are comprehensive and the options for management of those are valuable for clinicians.

The author refers to "figure" in the text but none is provided.

The second chapter deals with "standard" medical treatment of Parkinson's disease broadly without citing references.

The third chapter is on critical appraisal of Pergolide. It is very well written. The references need to be updated as some papers published 10 years earlier are still listed as "in press".

Chapter 4 on neuroprotection is, by and large, generalization of commonly available literature. The authors cite available evidence that Pergolide increase life expectancy and suggests that it may have neuroprotective effect.

As is the case with multiple authored books, there are some good chapters and every chapter contains some pearls. It is a good review, albeit tilted in favour of Pergolide. The references provided are in alphabetical order in some which I find difficult to read and sequentially as cited in other chapters.

It is a useful, short monograph for undergraduate and postgraduate students.

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MOLECULAR AND CELLULAR APPROACHES TO THE TREATMENT OF NEUROLOGICAL DISEASE. 1992. Edited by Stephen G. Waxman. Published by Raven Press, New York. 415 pages. $CDN 189.00 approx.

This book consists of 18 chapters by authorities in the field of neuronal injury and therapy, both pharmacotherapy and neural replacement therapy for CNS disease. After an erudite introduction by the editor, four sections follow concerning, respectively, mechanisms of neuronal injury and death, neuronal injury in specific disease states, therapeutic strategies, and cellular and molecular replacement. Molecular and cellular mechanisms are clarified by the authors of all chapters, in a manner that makes this book a must for the academic neurologist and the research neuroscientist with a clinical orientation. Although this book is a secondary publication, derived from a conference, new information is synthesized in a manner not possible in primary, peer-reviewed publications. The reader will thus be bought up to speed on calcium and glutamate-induced (excitotoxic) neuronal death, hypoxic and ischemic neuronal injury, free radical injury, grey and white matter ischemia, all in a manner bridging basic and clinical science. There are chapters on the role of excitotoxins in heredo-degenerative neurologic diseases, and steroid treatment of spinal cord injury. Therapeutic strategies covered include excitatory amino acid antagonism, hypothermia, calcium antagonism and modification of free radical production. Antisense nucleic acid technology and trans-gene expression in fibroblasts are also covered. Lastly, neural transplantation in the therapy of Parkinson's disease covers a field which will likely have clinical impact in the future treatment of at least one degenerative neurologic disease.

The editor states the approach in the book shall go from molecules to cells to patients, having an impact on diseases. This is a tall order indeed, transcending several levels of biological organization. As such, the usual array of complicated flow charts are present, some of which presume physiologic subcellular regulatory events to be automatically a part of pathophysiology. This is, however, in the nature of the discipline at the present state-of-the-art. No doubt as the field develops, specific mechanisms will dominate over others, and such charts will be simplified, concomitant with specific emerging therapies in neuroprotection. For those academic clinicians and basic scientists interested in neurologic disease, this book is indispensable.

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THE HEADACHES. 1993. Edited by Jes Oleson, Peer Tfelt-Hansen and K.M.A. Welch. Published by Raven Press, New York. 922 pages. $CDN 223.00 approx.

By any standards this is a monumental book and has the most encyclopedic approach to headache since the volumes on Headache in the Handbook of Neurology. It features a scientific approach to headache established by Harold Wolff and currently best exemplified by Jes Oleson who, along with Tfelt-Hansen and Welch, has carefully edited this volume by 121 authors from three continents. It is large (22cm x 29cm) so that it doesn't fit easily into a bookshelf beside other books in the well known Raven Press series, but rather like a coffee table book begs to be left open on the desk. The print is large and good use is made of diagrams and illustrations.

As with most multiauthored books it lacks the coherence of a single author text such as Blau's large but succinct volume, Wollf's Headache authored by Dalessio, or Lance's small but nonetheless complete book, which is, in my opinion still the most readable and useful book on the subject of headache. Even under the tight reign of Jes Oleson the huge number of authors results in a great heterogeneity of presentations. The choices of combinations of authors of each chapter seemed to have more political than scientific rational. I found that this lead to frustrating repetition and I had some difficulty finding specific information. For example the information on the influence of hormones on headache was scattered throughout many chapters.

Although very well organized, it perhaps follows too slavishly the Classification of the International Headache Society, developed