BOOK REVIEW

Fragile X syndrome

Fragile X Syndrome: Diagnosis, Treatment, and Research

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Fragile X is a fascinating subject for basic scientists and clinicians alike. Since it is a relatively common disorder, and the associated physical and behavioural abnormalities are moderate enough to allow affected individuals to participate at some level in all aspects of society, most pediatricians, teachers, pediatric therapists, and genetics professionals will care for individuals with Fragile X syndrome at some time during their careers. The advent of the prenatal diagnosis of Fragile X, with its technical problems and ethical concerns, has brought this condition into the realms of the obstetrician and ethicist as well. The scientific aspects of Fragile X may be even more interesting, since this syndrome involves several relatively recently discovered non-Mendelian genetic mechanisms and may become one of the first mental retardation syndromes to be completely understood at even the biochemical level. Accordingly, a variety of readers with widely disparate interests and goals need information on Fragile X. Although it is unusual for a single book to provide insight on all aspects of such a multifaceted condition, this one successfully does just that.

This is the third edition of this impressive book. Chapters concerning the diagnosis of Fragile X syndrome and past and current research are grouped into Part I, while Part II includes chapters discussing treatment, including pharmacotherapy, and emotional, behavioral, and academic interventions. Both sections are comprehensive, including both historical information and the latest updates. The reader who knows nothing about Fragile X is provided with enough background information to understand the relevance of current issues, and the knowledgeable reader will find a wealth of relatively new information concerning all aspects of this syndrome. Most chapters include a bibliography so comprehensive that it could probably fulfill the goals of a literature search for the avid reader.

The first chapter, on the physical and behavioral phenotype of Fragile X syndrome, is an extremely complete summary of the clinical aspects of Fragile X and includes helpful figures, photographs, and case histories. The chapter on the molecular biology of the Fragile X mutation begins with a simple and clear explanation of the DNA technology used to study and evaluate the mutation, which will allow readers without a scientific background to understand the more complicated molecular biology underlying the syndrome. The chapter on neuropsychology includes an interesting section on the developmental decline in IQ observed in

affected males along with an in-depth discussion of the pathology of various functional deficits. Other chapters focus on the functions of the FMR 1 protein, the epidemiology of the disease, and the use of animal models of Fragile X in current research. All the chapters in Part I have been updated to include the most recent data on various scientific or medical aspects of Fragile X, for example premature ovarian failure in premutation carriers, the likely cellular roles and mechanisms of action of the FMR protein, and the impact of abnormal synaptic pruning and maturation on brain function. Old and new data are presented logically and nicely integrated in each chapter, so that both the big picture and the important details are made clear.

Part II, containing chapters on the treatment of Fragile X, is similarly complete. It begins with a chapter on genetic counseling, which summarizes the key points, highlights likely counseling difficulties, and intelligently discusses testing options. The chapter on medical follow-up and pharmacotherapy will be especially useful for the nongeneticist clinician, because it discusses likely problems and appropriate therapy during each developmental period from infancy to late adolescence, and includes a thoughtful and complete discussion of pharmacotherapeutic options. Chapters on the treatment of emotional and behavioral problems and academic and other interventions are also thorough, presenting both current data and practical advice. The last chapter discusses the prospects for gene therapy, and includes a clear and cogent summary of the problems and limitations of current gene therapy techniques as well as their possible application to Fragile X.

The authors recruited to write the chapters are well-known experts in the field and, probably as the result of good editing, the styles of each chapter are uniform, facilitating the flow from one topic to the next. I have only two complaints, and each could easily be seen as a benefit rather than a drawback. The first complaint is that some of the scientific chapters may actually be too comprehensive. For many topics, the findings of multiple investigators researching the same issue are presented, often without the author's interpretation. In some places the results of each study are very similar and could easily have been summarized. In other places, the results are dissimilar, and are presented without comment regarding which findings are likely to be correct. For example, in a paragraph discussing the relation between the size of the Fragile X allele and the probability of expansion, the sentence 'the threshold for instability seems to be 35 pure CGG repeats', attributed to one source, is followed by a sentence stating 'the threshold for expansion to the full mutation is probably around 59 pure repeats', attributed to another source. The reader who already knows much about Fragile X may appreciate this compilation of information from a variety of sources, and be able to interpret it without difficulty, but the reader with no prior Fragile X knowledge may find the disparate data confusing. The other complaint is that five of the chapters begin with a reiteration of the basic facts concerning Fragile X, including history, inheritance, and phenotype, even though these subjects are discussed

very thoroughly in other chapters. This may be perceived as a benefit by some readers, since these chapters could more easily stand alone as a reference and be understood without the need to access additional background material. On the other hand, the reader who wants to read through the whole book may be annoyed by the repetition. These are small complaints, however, and should not deter any reader interested in learning the latest on Fragile X. This book provides a comprehensive

and well-written summary of what is currently known about this relatively common and fascinating disorder, and should be a valuable resource for readers with many different backgrounds and interests.

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