Book Reviews

Am. J. Hum. Genet. 74:781–782, 2004

Huntington's Disease, 3rd ed. Edited by Gillian Bates, Peter Harper, and Lesley Jones. New York: Oxford University Press, 2002. Pp. 558. $118.

The third edition of *Huntington's Disease,* edited by Gillian Bates, Peter Harper, and Lesley Jones, is dedicated to patients with Huntington's disease (HD) and their families. Compiled by leaders of HD research, this exhaustive and very informative review of the field is intended for the general reader.

Over the past 10 years, HD has attracted a large number of researchers and is now a standard subject in the syllabi of scientific and medical courses around the world, in large part because of its straightforward autosomal Mendelian inheritance pattern. After the mapping of its genetic locus in 1983, the genetic defect responsible for HD was identified within a decade by a team of basic scientists and clinicians. The identification of the defective gene gave scientists a great opportunity to understand its cellular and molecular biology by creating cell and animal models. The tremendous amount of progress toward understanding the pathogenesis of HD is reflected in the top-notch research that has been published.

A summary of HD research is admirably presented in the third edition of *Huntington's Disease*. It consists of 17 chapters organized into six sections; in each chapter, authoritative researchers comprehensively summarize past HD research and critically evaluate the current state of knowledge. This new edition contains six more chapters than the second edition.

Chapter 1 details the historical developments of HD, how present-day researchers can see the different areas of HD research evolving, and what their predecessors thought about HD. Chapter 2 deals with clinical aspects of HD, particularly early-, mid-, and advanced-stage disease phenotypes, motor abnormalities, and causes of death. Important issues, such as diagnosis, disease progression, and clinical severity, are addressed in this chapter. Chapter 3 provides a discussion of the neuropsychological and neuropsychiatric aspects of HD, with new information that cognitive and psychiatric symptoms result from the loss of cortical rather than striatal neurons. The fact that psychiatric symptoms are caused by the defective gene rather than the family situation is also discussed.

Chapter 5 describes the mapping and cloning of the *HD* gene. In this chapter, several other aspects of HD are also covered, including polyglutamine (or CAG) repeat expansion in different tissues, clinical correlation of CAG repeat sizes, genetic anticipation, and molecular mechanisms of CAG repeat expansion. This chapter is very informative for students of clinical genetics, molecular biology, and neurogenetics. The authoritative chapter 6, by Peter Harper (editor of the second edition), updates readers on the global prevalence of HD. This chapter is extremely useful for the planning of services for patients and families. Chapter 7 discusses the role of HD genetics in genetic counseling—particularly approaches to prediction, presymptomatic testing, and the importance of family history in risk estimation. In addition, this chapter provides information to family members of HD sufferers, and it also covers issues such as ethics and insurance of HD.

Chapters 8–10 describe the neurobiology of HD. Chapter 8 gives an impressive update of HD pathology, emphasizing that cell loss is not just confined to the basal ganglia but is found in cortical and subcortical regions. Chapter 9 summarizes neurochemical changes in the brain specimens of patients with HD, primate models, and genetically engineered mouse models. This chapter is truly outstanding in terms of the new information it provides on the alterations of neurotransmitters, neurotransmitter synthetic enzymes, receptors, and uptake sites in HD models. Chapter 10 covers the changes in energy metabolism in patients with HD, and it explains how metabolic deficits may lead to free-radical generation, the lowering of excitotoxicity, mitochondrial dysfunction, and apoptotic cell death.

Chapters 11–13 deal with structural biology, cell biology, and mouse models of HD. Specifically, the role of mutant huntingtin and its toxicity both in the cytoplasm and in the nucleus are discussed. Chapter 13, which describes the mouse models of HD, emphasizes aggregate formation, CAG repeat instabilities, neuronal degeneration and behavioral changes, gene expression changes, excitotoxicity, and oxidative damage. The development of mouse models not only has accelerated our understanding of HD biology but also has opened avenues to understanding other triplet CAG-repeat–associated neurological diseases, such as ataxias, spinal and bulbar muscular atrophy, and dentatorubral pallidoluysian atrophy.

Chapters 15–17 address the progress scientists have made toward therapeutic interventions for HD. Comprehensive care of HD is summarized in chapter 15, and chapter 16 reviews clinical trials of patients with HD. Chapter 17 describes the progress made toward cell transplantation in the CNS, striatal grafts in experimental rats, graft and host associations, preclinical studies in animals, clinical transplantation trials in patients with HD, and possible application of stem cell technology as a therapeutic strategy.

Without hesitation, I can say that this new edition provides an excellent summary of HD research and addresses the great promise of therapeutic interventions for HD. However, I still have to admit that we do not have a complete understanding of how mutant huntingtin targets specific regions of the brain and selectively kills a subpopulation of neurons, leading to

HD. Future research may find an answer to this critical issue and may provide more clues toward the development of therapy for HD. Overall, the third edition of *Huntington's Disease* provides the latest knowledge of HD and is extremely useful to the general reader; to students of human genetics, neuroscience, and neurobiology; and, of course, to clinicians and basic researchers.

P. Hemachandra Reddy
Oregon Health & Science University
Beaverton, OR

0002-9297/2004/7404-0021$15.00

Am. J. Hum. Genet. 74:782, 2004

Entwined Lives: Twins and What They Tell Us about Human Behavior, by Nancy Segal. New York: Plume, 2000. Pp. 396. $16 paperback, $27.95 hardcover.

As a human geneticist, I thought I knew a fair bit about twins, but I learned a lot more from this book, written by the director of the Twin Studies Center at California State University, Fullerton. The author's goal is "to bring twins and twin studies to life for the millions of people who will be more enriched, informed, and enlightened by the messages they hold."

As its subtitle suggests, the book deals mainly with intelligence and personality. It reviews the many studies that use the classical Galtonian approach of comparing MZ and DZ twin pairs raised together and apart. The consensus of these is that virtually everything examined shows some evidence of genetic influence. Intelligence and many of its subcomponents show high heritabilities, whereas estimates for personality traits tend to be lower, though always positive. Some summaries of the scientific findings in tables would have been useful.

But there are other kinds of twin comparison. Dr. Segal reviews the much-less-voluminous body of data from studies designed to get more of a handle on the environmental factors. There are "pseudotwins"—unrelated siblings (an oxymoron?) reared together of the same age, or UST-SAs. Their IQ scores are much less similar than those of MZ twins, DZ twins, and siblings, providing an estimate of how much (or little) the shared environment contributes to the similarity of people living together—one component of the heritability formula.

Studies of unlike-sexed versus like-sexed DZ twins are providing (somewhat conflicting) evidence of the effects of intrauterine exposure to hormones. Dr. Segal tells of superfecundated twins and children from eggs ovulated together but gestated separately (twibs?), which would provide other estimates of environmental effects, if enough twins could be evaluated.

Other aspects of twins and twinning that this book deals with include the "epidemic" of twinning resulting from assisted reproduction, twinning in nonhuman animals, conjoined twins, and clones.

Then there is the sociology of twinning. How do twins—and their families—feel about each other? Does a twin grieve more, or differently, for a lost cotwin than for a sib? Does the special bonding between twins have legal implications? There is a chapter on twin pairs who are outstanding academically (10 pages on the Shapiro twin university presidents), artistically, or athletically and a chapter on the heritability of athletic ability.

Interspersed with the scientific aspects of twin research are voluminous personal details—the life stories of selected twin pairs, reminiscences of Dr. Segal's conversations with them and their families, and personal revelations of her feelings about her own (DZ) twinship.

As the author points out, whereas classical twin studies estimate how much of our variation is due to genetic and how much to environmental factors, they do not identify these factors. They only tell us where to look. Analysis of environmental differences in discordant MZ pairs might identify causal factors, but this approach has not yielded much.

Dr. Segal suggests several new places to look, which (if one looks hard) may reveal implications for "our views of ourselves, our relationships with family members, our methods for raising children and our outlook on human potentials and possibilities."

The book should be a useful reference for geneticists, psychologists, and sociologists interested in the heritability of mental differences or in twinning itself. It should appeal particularly to members of the general public with a personal interest in twins—and who doesn't have one?

F. Clarke Fraser
Department of Human Genetics
McGill University
Montreal

0002-9297/2004/7404-0022$15.00