HUNTINGTON’S DISEASE
Third edition.
Edited by Gillian Bates, Peter Harper and Lesley Jones
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Huntington’s disease is a condition with devastating consequences both for patients and for their families. It is an autosomal dominant trinucleotide repeat disorder which codes for a mutant form of huntingtin and leads to a combination of motor, cognitive and affective signs and symptoms, death occurring 15–25 years after disease onset. Until relatively recently the condition was managed sympathetically with little realistic hope of offering anything much more than some palliative therapy, as and when this was required. However, since the discovery of the gene in 1993 and the realization that Huntington’s disease is part of a whole family of triplet repeat disorders, there have been great advances, and these are definitively laid out in this book. Originally devised by Peter Harper, the book is now in its third edition with an expanded editorship and 17 chapters that cover all aspects of the condition and reflect the way in which the field has moved forward in the last few years.

This new version of the book builds on the formidable reputation of the previous editions and is enhanced by the fact that the authors of each chapter are recognized experts in their field, and thus the accounts are authoritative. In addition, the book successfully links the basic scientific work on Huntington’s disease with the clinical experiences of patients with this condition. Indeed, the clinical chapters are to be recommended to all neurologists as they clearly lay out the issues facing patients with Huntington’s disease and the best approach to them; see, for example, the chapter by Martha Nance and Beryl Westphal. Sadly, though, most cases of Huntington’s disease are not seen in specialist clinics and so may receive suboptimal support, and even though such specialist Huntington’s disease clinics are starting to evolve they often fail to include all the necessary supportive services.

The book begins with a beautiful account by Peter Harper of the historical origins of the condition and also some of the earlier descriptions of it, which were overlooked until George Huntington put his name to this disorder. The book then discusses a number of clinical aspects of Huntington’s disease, the neurological aspects of the condition being comprehensively covered by Barry Kremer and the psychology and psychiatry by David Craufurd and Julie Snowden. In both these chapters the non-specialist is carefully negotiated through the field, and the major conclusions are clearly presented along with honest statements about what is known and not known about this disorder. These accounts lay the foundation for the imaging studies discussed by Thomasin Andrews and David Brooks from the MRC Cyclotron Unit in London. These researchers have been pioneering this area of Huntington’s disease research, which not only has proven to be informative in a number of different ways but may also serve as a useful biomarker in the clinic—one of the holy grails of Huntington’s disease research at the present time. Thus the imaging studies discussed in this chapter are referred to throughout the book, and the editors are to be congratulated on the way in which this has been done so clearly, without endless repetition of accounts.

The second section of the book deals with genetic aspects of Huntington’s disease and is probably more of interest to those who are involved in the counselling and testing of patients. Nevertheless, these accounts are very helpful for those not experienced in this particular aspect of Huntington’s disease management, as many of the issues touched upon in these chapters are commonly raised in clinical practice by patients and relatives. Thus, whilst one may not wish to know a lot about the counselling of asymptomatic, at-risk patients, it is always useful to be prepared as there is a very real risk of being ambushed on this topic by those accompanying the patients.

The third section of the book examines the neurobiological basis of Huntington’s disease through neuropathological, neurochemical and metabolic studies. These accounts are extremely informative, although some of them can be rather list-like and a little wordy without much in the way of illustration to break them up, which can put off the less determined reader. In general, the more successful chapters in this section of the book use well-placed and informative graphs or photographs. The absence of any colour illustrations in this edition is a shame, especially given that they add so much to the clarity of results from the imaging studies.

The fourth section of the book tackles the cell biology, detailing the pathophysiology of the disease in vitro as well as through transgenic mouse models. This is a fruitful area of
research, especially as it may reveal possible therapeutic interventions designed actually to slow disease progression, and so these chapters give great hope that new therapies will develop and enter the clinic. In this context, the inclusion of a chapter on other polyglutamine diseases was inspirational as it is becoming clear that many of these conditions have considerable overlap, with pathophysiological mechanisms in one disease leading to therapeutic interventions that will influence a whole host of disorders.

The final section of the book deals with therapies in Huntington’s disease. It is extraordinary how little we really know about the value of therapeutic interventions. For example, the chapter by Karl Kieburtz and Ira Shoulson on therapeutic trials in Huntington’s disease makes bleak reading as it repeatedly highlights the fact that there is little proper evidence for the treatment of most symptoms in this condition. There are very few controlled trials of any therapy, and thus the management of patients is very much based on anecdote and personal experience. The book concludes with an account by Anne Rosser and Steve Dunnett of the reparative approach to Huntington’s disease using cell and tissue transplantation. This approach is exciting but controversial, and has a tendency to split the Huntington’s disease community into those who believe it will never work, given the diffuse pathology of Huntington’s disease, versus those who believe that restoring striatal integrity will influence disease progression and symptomatology. At the moment this approach remains experimental and must be seen as one of many different strategies in the treatment of Huntington’s disease.

Overall the book is a magnificent collection of reviews on Huntington’s disease. It presents the information in an extremely readable and digestible form and is one of the very few neurological texts that I have read where I cannot wait to get on and read the next chapter, such is the interest and excitement that each account generates. Indeed, the honesty and breadth of coverage has certainly left me with a large number of research questions, which I now wish to explore in the laboratory and in patients. Of course, the field continues to move forward at pace and, as is bound to happen in books such as this, several key papers have emerged since this book was written; I have listed these below. Nevertheless, this third edition of Huntington’s Disease is terrific and should be read by anyone dealing with Huntington’s disease in whatever capacity, because it is without doubt the best book on the market about this condition.

Some key new references on Huntington’s disease since the publication of this book

Clinical genetics

Pathophysiology

Therapeutics

Roger Barker
Department of Neurology,
Addenbrooke’s Hospital NHS Trust,
Cambridge, UK
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