

## The force of prions



### Prion biology and diseases

Stanley B Prusiner, ed. *Cold Spring Harbor: Cold Spring Harbor Laboratory Press, 1999. Pp 794. US\$125.00. ISBN 0879695471.*

“The saga of prions truly represents the triumph of scientific investigation over prejudice.”

So reads the dedication of Stanley Prusiner to *Prion biology and diseases*. There are indeed many extraordinary aspects of this new biology of prions, not the least of which is their possible non-existence. Although the term prion tends to slide into as many reincarnations as the moment demands, we should adhere to the original definition if the concept is to be rigorously tested. Thus, prions are infectious “particles” composed of an abnormal form of a host protein known as prion protein (PrP). By definition, prions are devoid of nucleic acid and therefore require “unprecedented” mechanisms of replication and infection. Some of these presumed mechanisms and a large assortment of data on which they are based are set forth in this book.

The principal findings that lend most weight to the prion hypothesis are the original detection of PrP molecules in diseased brains, by Prusiner and colleagues, and the gene-knockout experiments which showed that PrP is required for infection by Charles Weissmann (University of Zurich, Zurich, Switzerland) and co-workers. Other claims, such as the lack of nucleic acids, or the transgenic recreation of infection, have not yet been reproduced outside of Prusiner’s laboratory—although this shortcoming is not discussed. Additionally, several laboratories including Prusiner’s, have produced abnormal PrP *in vitro*, but these preparations have also failed to infect animals. Much of these data may not be widely known, possibly because there is little impetus to publish negative findings.

Despite the fact that Prusiner was awarded the 1997 Nobel Prize for Physiology or Medicine for the discovery of prions, there is something unsettling in this book; only one side of the scientific coin is presented. Alternative explanations of data would have strengthened the book. For example, the diversity of infectious agents isolated from a single species, as well as the complexity of the “species barrier” do not fit demurely into any PrP paradigm. These issues are crucial because the evolution of the new bovine spongiform encephalopathy

infection and its ability to cross species barriers with shocking infidelity is of public concern. This behaviour is contrary to the predictions made for PrP. Indeed, this book frequently notes that abnormal PrP propagates poorly, if at all, unless it finds its own species likeness.

To solve these conundrums, and to deal with the difficulty of missing infectivity, Prusiner now creates a virtual factor called Protein X. This second protein initiates the infectious cycle and propels PrP on its pathological pathway. X sounds a lot like a virus.

Prusiner’s introduction covers all the themes and arguments in the “array of diverse topics” of later chapters, most of which are written by scientists who have worked, or work with Prusiner. The

book as a whole is less successful than some of the more carefully written papers on prions. By the end, an exclusive focus on PrP becomes confining as reiterated details are expanded beyond their natural limits or logical conclusions. This book is not like William Harvey’s monograph on the circulation of blood with its single liberating and clarifying bullet of beauty that still penetrates the physiology and structure of the heart.

*Prion biology and disease* is stimulating in ways probably not anticipated by its authors. It leads one to re-examine the objectivity of science and whether it is a myth vanished. It underscores the stunning force of the declarative sentence and, although I hate to admit it, the peculiarly American sport of betting on popular momentum.

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## Catching sight of movement disorders



### Movement disorders in clinical practice

Guy Sawle, ed. *Oxford: ISIS Medical Media, 1999. Pp 228 plus CD-ROM. £85.00. ISBN 1899066608.*

Despite the impact of modern diagnostic techniques, the cause, the pathology, or the genetic basis of many of the most common movement disorders are not known. An overview of movement disorders needs to attain a balance between the well-known clinical and neuropathological features and the uncertain significance of more recent immunocytochemical findings. Too much emphasis on one aspect of disease is one reason why books on movement disorders can be confusing. By contrast, going through *Movement disorders in clinical practice* was a pleasure!

In this book, disorders are grouped by occurrence (in childhood, in adults, or after exposure to drugs), and there is a chapter on those which occur during sleep, and one on miscellaneous disorders. Psychogenic disorders are discussed separately. Therapy is considered together with each disorder, except for Parkinson’s disease, which has a special chapter on neurosurgical treatment.

Clinical descriptions are always comprehensive and clear, and the video clips on CD-ROM are of good quality, and well-selected and coordinated with the text. Most clips give a realistic illustration of the clinical findings of each

disorder—an advantage over straightforward descriptions. Thus, the relevance of the skilled clinical examination is acknowledged without neglecting the reality of making diagnoses by pattern recognition.

The correlation of clinical and histological findings is not a simple task in movement disorders—even for common disorders, such as Parkinson’s disease. So it is helpful for the clinician, who lacks neuropathological experience, to obtain critical and comprehensive statements on the important histological features. The neuropathological slides are of excellent quality, the relevant immunohistochemical stains are covered, and the mismatch between clinical diagnosis during life and the neuropathological diagnosis are critically discussed.

I would recommend *Movement disorders in clinical practice* to the student and to every neurologist who needs a quick and solid update on information, or help with differential diagnoses.

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