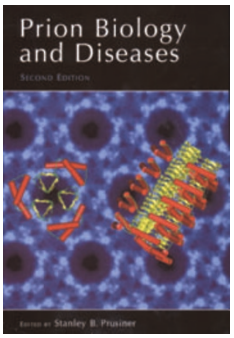
BOOKS

Prion's progress



Prion Biology and Diseases, Second Edition

Edited by Stanley B. Prusiner

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The prion hypothesis, so heretical when first systematized by Stanley Prusiner, is now the standard model to account for the infectivity of the transmissible spongiform encephalopathies (TSEs) — a class of infectious diseases characterized by neuronal degeneration, spongiform change, gliosis and accumulation of amyloid protein deposits. The prion hypothesis posits that TSE infectivity comprises the conformational conversion of the host-encoded cellular prion protein PrP^{C} into the disease-associated isoform PrP^{Sc} (its generic name). The agents that transmit TSEs thus differ from all other microbes in that no agent-specific nucleic acid is required for agent "replication." The once radical notion that protein conformational change may be propagated in a templated conversion event, a process more akin to crystallization than replication, has now achieved near-universal assent. This hypothesis is also attaining unpredicted utility in elucidating aspects of normal and abnormal biology of organisms as diverse as yeast and man.

The prion hypothesis has also journeyed beyond its academic roots to acquire a practical urgency in the world today. Perhaps a novelty only to denizens of desert islands, prions and prion diseases are now of critical concern to physicians, veterinarians, economists and politicians, as well as the populations they serve. Human prion diseases, which are uniformly fatal, include classical Creutzfeldt-Jakob disease (CJD), which has sporadic, iatrogenic and familial forms. Since 1996, a new variant of CJD (vCJD) has been identified in the UK, France, the Republic of Ireland, Hong Kong, Italy, the US and Canada. vCJD, which has afflicted around 150 individuals so far, is almost certainly the result of oral transmission of bovine spongiform encephalopathy (BSE). At the time of writing, the probable transmission through blood transfusion of vCJD to two patients in the UK has raised the spectre of a "secondary epidemic" of vCJD that could dwarf the first. The discovery last year of two BSE cattle in previously unaffected North America has precipitated economic disaster for cattle industries, and has provoked widespread public disquiet in the US and Canada. Chronic wasting disease of deer and elk continues to emerge as a worrisome home-grown BSE homologue.

Because of the increasing importance of prions to public health, and the burgeoning rate of discovery in prion biology, this is a timely occasion for an second edition of the book *Prion Biology and Diseases*. As with the first edition (published in 1999), the extensively revised and updated second edition is edited and substantially written by Stanley Prusiner. A group of international experts have collaborated with the editor to produce an authoritative book that includes chapters by many of the masters in the field. The initial section on prion biology includes the classical material present in the earlier edition, with the addition of two important late-breaking developments: remarkable new work on the left-handed β-helix structure of PrP 27–30 (by Cédric Govaerts *et al.*), and an entirely new chapter, *Doppel, a New PrP-like Mammalian Protein* (by David Westaway *et al.*). A fascinating chapter by Reed Wickner, Susan Liebman and Sven Saupe — *Prions of Yeast and Filamentous Fungi* — has also been updated to include new data extending the prion principle as a non-genetic mode of inheritance important in yeast viability and fungal heterokaryon incompatibility. The chapter *Cell Biology of Prions* by David Harris, Peter Peters, Albert Taraboulos, Vishwanath Lingappa, Stephen DeArmond and Stanley Prusiner includes new material on prion protein synthesis, trafficking and degradation. Remarkably, scientific contradiction among the authors of this chapter is deliberately highlighted and attributed, as if to signal that the field is now sufficiently established to tolerate such controversy. Sections on prion diseases in humans and animals contain comprehensive and current reviews of these areas. Finally, a section on methodology, biosafety and therapeutics includes expanded and previously unpublished data on prion detection and therapeutic approaches, in chapters lead-authored by Prusiner.

The book is comprehensive, authoritative, accessible and, for the most part, exciting to read. It will serve admirably as a standard of the new science of "prionology" for scientists, physicians and students. As with any omnibus, there are shortcomings. Certain contributions (and contributors) to prion science are overlooked, and a useful chapter has been extirpated from the first edition for reasons that elude me (R. Anthony Williamson and colleagues, *Antibodies as Tools to Probe Protein (PrP) Biology*). Stylistically, there is redundancy in some chapters, possibly to enable each chapter to stand on its own, but vexing on a cover-to-cover reading.

It seems fair to ask of the prion hypothesis, as impatient kids do on road trips, "are we there yet?" In July this year, the Prusiner laboratory published a paper seemingly demonstrating the creation of infectious prions from recombinant prion protein *in vitro*. With this one spectacular experiment, it seems possible that we are nearing the end of the beginning of prion research. But even if the skeptics are silenced, there will, of course, be residual questions. How does prion protein conversion occur? How general is the prion hypothesis ? How do prions kill neurons? What is the function of the cellular prion protein? And perhaps most critical – for a scientific problem whose origin dwells in the rag-and-bone shop of human and animal disease – how can these disorders be efficiently diagnosed and effectively treated? These questions are the signposts for the next few decades in the journey of the extraordinarily fruitful prion hypothesis, and will surely form the basis for new volumes on this topic.

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