Prions. A challenge to Science, Medicine and the Public Health System

Second edition (revised and extended). H.F. Rabenau, J. Cinatl, H.W. Doerr eds. Basel: Karger, 2004. ISBN 3-8055-7656-0. 222 pp. US$162.

In a seminal paper in 1965, Dickinson demonstrated that scrapie in sheep, the archetype of transmissible spongiform encephalopathy (TSE) or prion diseases, was caused by an infection, but with susceptibility and incubation period under the genetic control of the host. Despite the subsequent failure of much of the published research in the field to take account of this fundamental finding, measures to control TSE disease problems, including bovine spongiform encephalopathy (BSE), have correctly and fortunately been based on this fundamental insight – as Bradley illustrates in his comprehensive chapter on the discovery of BSE, the resulting research and ultimate control of the BSE epidemic.

Conceptually, the BSE epidemic has been relatively easy to comprehend and control measures simple to recommend. There was a single mechanism of infection arising out of modern agro-industrial practice – the contamination of meat and bone meal (MBM), obtained from BSE-infected animals, by an infectious agent which survived heat processing in sufficient amounts to infect animals given feed incorporating MBM. The difficulties of controlling BSE have arisen from the involvement of that most complex of vectors, man.

Sometimes we have resisted acknowledging the possibility of BSE within arbitrary geographic areas, we have resisted implementation of the best diagnostic tools of the time, and so the epidemic has grown needlessly. Sometimes we have not faced up to the potential dangers of BSE or short-term economic drivers and human laziness, which lead to imperfect implementation of confusing regulations and so prolong the epidemic.

In addition to the privilege of working on a unique scientific problem, scientists in the TSE field have had to work with bureaucrats, politicians and the press to meet the challenge of BSE in order to develop effective control measures. It is an aim of this book, Volume 11 in the *Contributions to Microbiology* series, to address the challenge of BSE to the public health system. Some of the data used to develop policy are reviewed but the book fails to convey adequately an understanding of the development of policy to control BSE by the UK, the EU or other national or international bodies.

Fortunately, BSE has infected humans only in very low numbers so far, although the analysis of various risk factors suggests that other genetic subgroups may be incubating primary BSE infection. Human-to-human transmission through blood transfusion has been identified and transmission via other mechanisms (e.g., blood products or contaminated surgical instruments) remains a possibility. Identification of potential transmissions of BSE required a thorough understanding of extant TSEs in humans. So it was clear when the first transmissions of BSE to humans were suspected that a new form of TSE had been identified and variant Creutzfeldt-Jakob disease (vCJD) was described. Confirmation that vCJD was in all likelihood caused by BSE transmission came from strain typing (i.e., comparison of phenotypic properties of TSE isolates). The established methods, originally developed by Dickinson, demonstrated convincingly the similarity of BSE and vCJD isolates, and these data were supported by the similarity of distinguishing properties of pathological forms of the host prion glycoprotein (PrP).

Underlying the implementation of practical advice on controlling TSEs has been the desire to understand the structural and functional properties of the causal agents of these diseases. Debate has centred on the protein only (prion) hypothesis, in which the structure of the causal agent is predicted not to contain nucleic acid, but that information transmitted from one host to another is encoded by conformational change to the host PrP protein.

The primacy of the prion hypothesis is accepted by the editors to such a degree that they have eliminated from the second edition the only chapter that previously offered any critique of the prion hypothesis. In its present state of evolution, the prion hypothesis fails to account for known functional properties of TSE agents, notably their ability to determine incubation periods and to specify the targeting of pathological lesions, which allow strains to be differentiated.

Clearly, either the prion hypothesis must be developed to account in detail for how these properties are encoded in the structure of the infectious agent and expressed in the infected organism, or the hypothesis is invalid and other hypotheses based on conventional mechanisms should be developed. It is sad that the editors have failed to appreciate the fundamental challenges to the understanding of the transmission of biological information that TSEs bestow on the scientific community.

Overall, the book summarises much information required to understand the present state of TSEs from a medical and veterinary perspective. However, it explains less adequately how this information has been used to develop formal assessments of the risks TSEs now pose or how this information has been used to develop policy, nor does it effectively meet the challenge that the fundamental properties of TSEs offer to modern biological science. □

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