Prions
A Challenge for Science, Medicine and the Public Health System
2nd, revised and extended edition

Volume Editors

Holger F. Rabenau Frankfurt/Main
Jindrich Cinatl Frankfurt/Main
Hans Wilhelm Doerr Frankfurt/Main

26 figures, 2 in color, and 19 tables, 2004
Contents

VII Dedication in Remembrance of Andreas Scheid (1941–2001)
Schmidt, A. (Wuppertal)

VIII Note of the Series Editor
Schmidt, A. (Wuppertal)

IX Preface to the Second Edition
Rabenau, H.F.; Cinatl, J.; Doerr, H.W. (Frankfurt/Main)

X Preface to the First Edition
Rabenau, H.F.; Cinatl, J.; Doerr, H.W. (Frankfurt/Main)

1 Transmissible Spongiform Encephalopathies: The Prion Theory –
Background and Basic Information
Riesner, D. (Düsseldorf)

14 Structural Biology of Prions
Cappai, R. (Melbourne/Parkville); Collins, S.J. (Parkville)

33 Prion Strains and Species Barriers
Hill, A.F.; Collinge, J. (London)

50 Prions of Saccharomyces and Podospora
Baxa, U.; Taylor, K.L.; Steven, A.C.; Wickner, R.B. (Bethesda, Md.)

72 Human Prion Diseases: Cause, Clinical and Diagnostic Aspects
Knight, R. (Edinburgh); Brazier, M.; Collins, S.J. (Parkville)
Dedication in Remembrance of
Andreas Scheid (1941–2001)

Andreas Scheid, PhD, MD, University Professor, virologist and physician, was an outstanding scientist in influenza research at Rockefeller University, USA, and later on the Director and Head of the Institute of Medical Virology at the Heinrich Heine University of Düsseldorf, Germany. He also had a lot of interests, especially in cultural aspects, such as being an dedicated musician.

Andreas, you left us far too early due to a severe, very long-lasting and painful disease. I am very indebted to you as my personal teacher in virology. You gave me a lot of advice in virology, especially in our exchanges from physician to physician and as a personal friend.

Axel Schmidt
Series Editor
Note of the Series Editor

New emerging pathogens and/or infectious agents are a main scope of the Karger book series *Contributions to Microbiology*. 

Prion-associated diseases such as BSE and other spongiform encephalopathies are a major and worldwide focus of interest at the moment, ranging from sciences, over politics and public media, to the ‘worried’ consumer of meat and meat-associated products, as probably the majority of us are.

I would like to express my special thanks to the highly competent and experienced volume editors Holger F. Rabenau, Jindrich Cinatl and Hans Wilhelm Doerr, all at the Institute of Medical Virology, Johann Wolfgang von Goethe University, Frankfurt am Main, Germany, who already edited the first and extremely successful 7th volume of *Contributions to Microbiology*, published in 2001. They convinced and engaged outstanding and internationally recognised scientists and experts in the corresponding fields to contribute excellent chapters for the present volume. Due to the tremendous success and acceptance of the initial exciting volume of *Contributions to Microbiology*, the preparation of a second, completely revised, updated and extended edition became mandatory. Again to the editors: my personal thanks to you for once more taking on this new challenge. Moreover, I also personally thank Karger Publishers for their kind and very supportive and professional collaboration with the project.

This edition of the volume provides a very comprehensive and updated source of information on all aspects of prions and prion-associated diseases that has been derived from very different viewpoints concerning spongiform encephalopathies. Many novel and ‘up-to-date’ aspects are presented which have not been included in other textbooks so far and in such a comprehensive way, which in turn will inevitably lead to a higher and more sophisticated awareness of the present situation concerning the ‘prion problem’.

*Axel Schmidt*, Series Editor
Witten/Herdecke, November 2003
Preface to the Second Edition

This book was initiated and edited by general microbiologists or virologists, who had numerous questions concerning prion origin and replication, virulence and pathogenicity, diagnosis and therapy, transmission and susceptibility, as well as inactivation and prevention. Although the rapid progress of research had outdated the ‘state of the art’ at the time of publication, those questions were of such common interest that the book was soon sold out. Now, three years later, a second approach to these issues is presented. The protein-only hypothesis on prions is now commonly accepted, although there are some reservations. Therefore, the contribution dealing with arguments against this hypothesis was not rewritten. While the BSE epidemic has declined, the number of new, i.e. variant Creutzfeldt-Jacob disease cases has risen. Although it will probably not reach the features of an epidemic in humans, the challenge for science, medicine and public health is always present. After the first American case of BSE emerged in a cow that had not been imported, the question about an endogenous or exogenous origin of disease has again been raised. Our knowledge of prion biology has considerably improved covering both human, animal and even microbe affections. Beside some insights in basic research, the second edition emphasizes practical aspects of fighting human and animal prion diseases. Additionally, chapters on public regulations of this issue and on veterinary measures were included. The volume editors wish to thank Karger Publishers and the series editor of Contributions to Microbiology for encouraging this second edition.

Frankfurt am Main, November 2003

The Volume Editors
Preface to the First Edition

After the great successes of modern hygiene and medical microbiology, many people thought the threat of infectious diseases had disappeared. However, emerging and re-emerging infections with more or less pathogenic potential disproved this opinion. The onset of the AIDS epidemic has brought the old problem of slow virus diseases to general attention. For many years, it had been postulated that some of those diseases, particularly of the brain, were caused by unconventional viruses. Infections with these agents do not induce classical inflammations – acute or chronic encephalitis due to a specific immune reaction – but a slow and irreversible degeneration of the central nervous system presenting as encephalopathy. Those diseases had been considered rare events in animals and humans, only interesting medical and veterinary doctors and scientists – scrapie in sheep and Creutzfeldt-Jakob disease (CJD) in man were known only to specialists. The onset of the bovine spongiform encephalopathy (BSE) epidemic in Great Britain completely changed the situation. The fatal risk of consuming contaminated beef became a topic. And indeed, the fears were materialized when the first cases of new variant CJD (vCJD) were identified.

From the scientific point of view, it was a real sensation, when infectious agents without any nucleic-acid-based genome were hypothesized, which were later called proteinaceous infectious organisms (prions). The dogma that self-replicating biologic agents depend on genomic information conserved in the sequence of nucleic acids had to be given up. However, it should not be forgotten that prions are real ‘viruses’ (in the original sense of toxic material),
as defined by the very early virologists. A lot of questions arose: How do those agents replicate? Do they always harm the host? Which factors of virulence can be identified? What are the mechanisms of pathogenicity? How are the agents transmitted? What are the options of early laboratory diagnosis and development of therapy and prevention?

In this edition of Contributions to Microbiology, leading scientists in different fields of biomedical research show once again how important it is to deal with the prion ‘problem’ in a multidisciplinary manner. The long-lasting discussion about the virus or prion theory is getting a clearer background. Furthermore, the structures of prions and their molecular biological analysis, and the questions of strain variations and species barrier are discussed. Another chapter tells us what we can learn about prions from yeast experiments. The possibilities of inactivation and disinfection of prions are of great importance for public health. This includes the test methods and their problems as well as the recommendations for clinical use and official regulations.

Another part of this book concentrates on the causes and clinical diagnostic aspects of TSE. While previously vCJD could be diagnosed only postmortem, new tests now allow identification of the disease with some confidence while victims are still alive (at least 1 year before its clinical onset). The tests include tonsil and appendix biopsies and magnetic resonance imaging. Furthermore, the epidemiology of human and animal prion diseases, disease management and the risks to public health or biologists (e.g. in the pharmaceutical industry) are also discussed.

In summary, this book informs about the state of the art of prion infection and disease.

Frankfurt/Main, May 2000

Holger F. Rabenau
Jindrich Cinatl
Hans Wilhelm Doerr