Prions in Humans and Animals

Edited by Beat Hörnlimann, Detlev Riesner, and Hans Kretzschmar
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Edited by
Beat Hörnlimann

in collaboration with
Detlev Riesner and Hans Kretzschmar
To Fabian and Nadine for their encouraging support, and a humble apology for the innumerable hours of neglect

Beat Hörlimann, Chief Editor

To William J. Hadlow for his important contribution to the interdisciplinary cooperation in the research on prion diseases

The Editors
Wisdom

What lies behind us
and what lies beyond us
are tiny matters compared to what lies within us.
And when we bring what is within out into the
world, miracles happen.

Henry David Thoreau
The idea of writing the first edition of this book came to me on 1 September 1994 in Paris during a TSE conference at the OIE. Two years later, inspired by the following passage from Goethe’s Faust the project began in earnest:

*Oh, happy, he who still can hope
To rise from this chaotic sea of errors!
What you don’t know, is always what you need
And what you know, you have no use for.*

After the successful publication of the German-language edition, and as BSE continued to spread around the globe, the editors made the decision to publish an English-language edition in order to reach more scientists and decision-makers.

The scientific fascination of prions and prion diseases was the motivating force in publishing this book. From the very beginning, our goal was to present the historical dimension as well as the scientific, medical, veterinary, and practical viewpoints on prions, their resulting diseases, and their containment. Given that these fields are closely interwoven, the task of bringing the whole project together has been a complex one. I am proud to say that this goal has been achieved and a solid and scientific source of information has now been realized for the second time.

The book is intended to be a unified text and not just a collection of individual contributions. The first section of the book deals with the fundamental historical, medical, and scientific background, while the second section focuses on the practicalities of the subject. The book demonstrates the complex interactions of the many facets of prion diseases. The extensive text is interspersed with numerous detailed figures and tables.

I wish to express my sincere gratitude to all those who took part in the realization of this mammoth project, throughout the writing of which there has been an excellent esprit de corps. First of all, I thank Terry Berger for her unflagging support and friendship during my time devoted to the completion of the present edition.

I have had the pleasure of working with two outstanding co-editors, Hans and Detlev. Furthermore, eighty internationally-renowned co-authors contributed to the book and I wish to express my sincere thanks to each and every one of them.

Scientific reviews were carried out by a group of excellent specialists listed below, who checked the quality of content. By contributing their knowledge, the book has become very much a joint oeuvre. My very special thanks go to Stuart C. MacDiarmid and Michael P. Alpers.

In particular, I would like to thank Jutta Bachmann and her team in Norway for their excellent support in translating numerous chapters of the present book. The cooperation with her was characterized by her expert knowledge of the subject matter as well as by an unparalleled cordiality. I could not have envisaged a more suitable institution than Bachmann Consulting to have worked on these scientific texts.

I also wish to thank various other institutions and colleagues who offered their support in many different ways. Further thanks go to the writer of the introductory text, Nobel laureate Werner Arber.

My special thanks also go to the publishing house Walter de Gruyter, in which we have been fortunate to have found a most competent publisher; particular thanks go to Wolfgang Böttner and Stephanie Dawson.
It has been an honor to oversee the project from its conception. The realization of this and the former edition (Prionen und Prionkrankheiten, 2001) made my role as chief editor a rewarding experience. This venture has only been possible with the help of my family. Therefore, I thank Eva Hörlimann and our children Fabian and Nadine.

December 2006

Beat Hörlimann, Chief Editor
Beside the authors, the following persons have supported the editors:

General Support
Berger, Terry, Oberrüti, Switzerland
Gruber, Heidi, Düsseldorf, Germany
Hansen Gerheuser, Linda, Windisch, Switzerland
Hartmann, Diethelm, Bern, Switzerland
Häring, Petra, Auw, Switzerland
Holl, Walter, Ebikon, Switzerland
Hörnlimann, Charlotte¹, Engelswil, Switzerland
Hörnlimann, Eva, Oberrüti, Switzerland
Hörnlimann, Fabian B., Oberrüti, Switzerland
Hörnlimann, Nadine E., Oberrüti, Switzerland
Hörnlimann, Paul¹, Engelswil, Switzerland
Käppel, Reinhard, Frankfurt, Germany
Kürsteiner, Dorli, Goldach, Switzerland
Kürsteiner, Georg, Goldach, Switzerland
Lederer, Rosi, Munich, Germany
Rogive, Colette, Bern, Switzerland
Schenk, Jeannette, Auw, Switzerland
Zeltner, Thomas, Bern, Switzerland

Graphics and Setting
Speidel, Christel, Berlin, Germany
Suter, Print AG, Ostermundigen, Switzerland
Tutte, Druckerei GmbH, Salzweg, Germany
Zech, Martin, Bremen, Germany

Literature and Index
Müller, Isabelle, Bern, Switzerland
Oesch, Bruno, Schlieren, Switzerland
Stahlkopf, Jens, Berlin, Germany

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Alpers, Michael P., Curtin University of Technology, Perth, Australia & The Kuru Surveillance Team, Papua New Guinea Institute of Medical Research, Goroka, PNG
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www.jbachmann-consulting.com

¹ Except for D. Carleton Gajdusek (reviewed Chapter 2 in the first edition) and Colin L. Masters (reviewed Chapters 1; 26 & wrote epilogue)
The book was made possible through the support of:

**Baxter BioScience**  
Global Pathogen Safety  
Industriestr. 67  
A-1220 Vienna, Austria

**Canadian Ministry of Agriculture**  
Ottawa  
Ontario K1A 0A6, Canada

**Dr. Weigert GmbH & Co. KG**  
Muehlenhagen 85  
D-20539 Hamburg, Germany

**Desopharmex AG**  
Pharma- und Medizintechnik  
Mutenstr. 107  
CH-4133 Pratteln, Switzerland

**Friedrich Oberthür**  
Stiftung  
Walbruch 1  
D-49844 Bawinkel, Germany

**Johnson & Johnson Medical**  
Rotzenbuehlstr. 55  
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**Novartis Pharma AG**  
Policy and External Affairs  
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**US Department of Agriculture**  
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**Prionics AG**  
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CH-8952 Schlieren, Switzerland

**Swiss Federal Public Health Office**  
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Foreword

Until the middle of the 1980s, prions were not accepted as a new infectious entity by the scientific community. At that time, research on prions still remained an area of largely esoteric interest. However, as a result of the BSE crisis, prion research has gained more attention in science, medicine and agriculture and has influenced politics and economics – with an impact in more or less every field related to consumer behavior. To the public the problems became obvious through media headlines about “BSE”, “Mad Cow Disease” or “variant Creutzfeldt-Jakob-Disease”, and in the scientific community a new field of multidisciplinary research has emerged.

The perspectives on prion research are as manifold as the readership which the editors and authors would like to reach. This book addresses readers from human and veterinary medicine, the biological disciplines such as molecular biology, biochemistry, and biophysics, agronomics and epidemiology – regardless of whether they are practitioners, students or work in research and education. In addition, experts from areas such as public health, governmental control agencies and the food and drug industry will also benefit from this systematic treatment.

To this end, the editors would like to express their gratitude to all authors who have contributed to this project. Most of them have been working in this field for years and are internationally renowned. Such a firm foundation helps to guarantee the scientific integrity of the presentation. The first edition of this book appeared in 2001 in German. Thanks to its wide acceptance, the editors felt prompted to work on a second edition, but this time in English – in order to reach a more international audience. Authors of the first edition updated their contributions and further authors joined the group of contributors.

Our goal was to present an extremely complex field in a language comprehensible to all. Repetitions are restricted to those parts in which new relationships are described or details expanded. We have aimed to focus on clear, definitive statements wherever possible. The book also provides information on existing gaps in our knowledge: hypotheses and assumptions are indicated as such.

We hope that this book will lead to innovative research ideas, further interdisciplinary cooperation in the research on prion diseases, and effective containment of disease.

The Editors

Beat Hörnlimann

Detlev Riesner

Hans Kretzschmar
Preface by Werner Arber

Research into prions and the diseases caused by prions has largely been marked in the past few decades by innovative findings in molecular genetics and the study of protein functions. The results gained from prion research represent a very interesting example of an in-depth insight into the complexity of gene functions and the interactions between biologically-active macromolecules.

Until recently, as a result of poor understanding of the subject, this natural complexity did not receive the attention that it was due, especially from the sciences. With regard to genetic information, this was related to a belief in science that genes “programmed” the processes of life in a very strict way, i.e., exactly “determined” the processes of life. In this extreme formulation, this view is not correct and needs to be corrected both within the scientific community as well as in the increasingly important dialogue with the public.

The limits of genetic predetermination depend, in part, on the natural structural flexibility of biologically active macromolecules. These include proteins, which, as the products of genes, influence the processes of life in many ways. Of course, this influence depends on the structural conformation of the proteins. Depending on their primary structure, i.e., their amino acid sequences, proteins can, in general, adopt several different tertiary structures, each being characterized by a certain, sometimes high, stability. The chances of adopting different conformations can depend on external factors, in particular on the effect of other protein molecules, which are then called chaperones or helper proteins.

The example of prions shows that a given protein molecule can efficiently influence the structure of another protein of the same kind. In addition, it shows that life functions and dysfunctions caused by prions are largely influenced by the conformation of the prion protein. It is, therefore, important that the scientific community make it clear to scientists and the general public that many processes of life are influenced by probabilities and uncertainties.

The present book represents an important contribution to the comprehension of the concept outlined here. At the same time it informs the interested reader on the current state of prion research.

Werner Arber
Professor Emeritus of Molecular Microbiology at the Biozentrum, University of Basel, Switzerland

In 1978, Professor Arber was awarded the Nobel Prize for Medicine or Physiology for his findings on restriction enzymes and their use in molecular genetics.
# Table of Contents

Abbreviations ........................................... XXV

**Topic I: History**

1 Historical Introduction ......................... 3  
   *B. Hörlimann, D. Riesner, H. Kretzschmar,*  
   *R.G. Will, S.C. MacDiarmid, G.A. H. Wells,*  
   *and M. P. Alpers*
   
1.1 Introduction ..................................... 3
1.2 The cause of prion diseases ...................... 3
1.3 Scrapie: archetype of all prion diseases ....... 4
1.4 Transmissible mink encephalopathy ............ 7
1.5 Chronic wasting disease in North American cervids ................................. 7
1.6 Creutzfeldt-Jakob disease and other human prion diseases .................... 8
1.7 The scrapie-kuru connection .................... 11
1.8 Etiological variety of prion diseases ......... 12
1.9 New prion diseases ............................... 14
1.10 Prion diseases and contagion ................. 18
1.11 Summary: traits common to all human and animal prion diseases ......... 18
1.12 Synopsis of events, discoveries and findings since 1732 ..................... 19

2 History of Kuru Research ....................... 28  
   *B. Hörlimann*
   
2.1 Introduction ..................................... 28
2.2 From the stone age to the present: the Fore people ......................... 28
2.3 Discovery of kuru ............................... 29
2.4 The “Tukabu” ritual ............................ 32
2.5 The beginning of kuru research ................ 32
2.6 A kuru hospital in Okapa ....................... 33
2.7 The spread of kuru .............................. 34
2.8 The pathological picture ....................... 35
2.9 The diet of the Fore ............................ 36
2.10 The geographical spread of the epidemic and the phylogenetic relations among kuru victims .................................................. 37

2.11 The ancestral cult ............................. 38
2.12 Social impact ................................. 39
2.13 The discovery of transmissibility .......... 40
2.14 The answers to the questions ............... 41

3 History of Prion Research ..................... 44  
   *S.B. Prusiner*
   
3.1 Introduction ..................................... 44
3.2 Animals and humans affected ................. 44
3.3 In search of the cause ......................... 46
3.4 Amazing discovery ............................. 46
3.5 Prion diseases can be inherited .......... 47
3.6 One protein, two shapes ...................... 51
3.7 Treatment ideas emerge ....................... 51
3.8 The mystery of “strains” ...................... 52
3.9 Breaking the barrier ........................... 53
3.10 The list may grow ............................. 54
3.11 Striking similarities ......................... 54

**Topic II: Molecular Biology and Genetics**

4 The Physical Nature of the Prion .......... 59  
   *D. Riesner*
   
4.1 Introduction ..................................... 59
4.2 The prion model and its nomenclature .... 59
4.3 The virus hypothesis ......................... 60
4.4 The virino hypothesis ......................... 61
4.5 The nucleic acid problem ..................... 61

5 Folding of the Recombinant Prion Protein ........................................... 69  
   *R. Glockshuber, J. Stöhr, and D. Riesner*
   
5.1 Introduction ..................................... 69
5.2 Folding of recombinant PrP<sup>C</sup> .......... 70
5.3 The role of the single disulfide bond of PrP ........................................ 73
5.4 Influence of point mutations linked with inherited human prion diseases on the thermodynamic stability of recombinant PrP<sup>C</sup> 74