

In Summary...

from the **INSTITUTE OF MEDICINE**

Shaping the Future for Health

ADVANCING PRION SCIENCE: GUIDANCE FOR THE NATIONAL PRION RESEARCH PROGRAM

PRIONS: RADICALLY NEW PATHOGENS

Unlike viruses and microorganisms — the agents of most known infectious diseases — prions are an abnormally shaped form of a normal mammalian protein. Identified in 1982, prions appear to be associated with the uniformly fatal neurodegenerative diseases called transmissible spongiform encephalopathies (TSEs). Conventional methods used to diagnose most infectious diseases fail to detect TSEs.

Detect Prion Disease Early

Prion diseases incubate for months to decades. The human prion disease kuru incubates for four to 40 years. Clinicians must be able to detect prion disease during the incubation phase.

There is no cure, prophylaxis, or fail-safe antemortem diagnostic test for

TSEs. A decade's worth of attempts to develop effective prion-detection tests have largely failed. Consequently, the U.S. Department of Defense launched the National Prion Research Program in 2002 with \$42.5 million and asked the Institute of Medicine to provide a research agenda for the first round of grants. *Advancing Prion Science: Guidance for the National Prion Research Program* is that agenda. It is the interim report of the Committee on Transmissible Spongiform Encephalopathies: Assessment of Relevant Science, whose members are listed on the reverse.

RECENT OUTBREAKS CREATE CONCERN

The 1985 outbreak of mad cow disease in the United Kingdom generated global awareness of TSEs. Mad cow is a prion disease called bovine spongiform encephalopathy. Human consumption of beef products from cattle that had mad cow disease apparently gave rise to a new TSE in humans, variant Creutzfeldt-Jakob disease (vCJD), identified in 1996. Today, deer and elk in the Midwest United States and in Canada suffer from an epidemic of yet another TSE, chronic wasting disease. It is unclear how chronic wasting disease is transmitted among deer and elk, or whether human consumption of infected deer or elk tissue could cause a TSE in people.

THE CHALLENGE:

Develop an antemortem diagnostic test for TSE

The committee recommends a number of strategies, including the two below, for achieving a rapid diagnostic test that is sensitive and specific enough to detect minute amounts of prions without producing false-positives.

- ★ Develop novel methods and reagents that detect or bind to prions, including new antibodies, peptides, nucleic acids, synthetic derivatives, and chimeric molecules. This may lead not only to better diagnostics, but also to therapeutic and prophylactic strategies.
- ★ Identify surrogate markers or signatures for the detection of prions or prion diseases.

But the committee concluded that without a better understanding of prions and their normal cellular counterparts, it will be virtually impossible to achieve the desired TSE diagnostic tests. So the committee has recommended that the DoD program **fund basic research** into the structural features of prions, the molecular mechanisms of prion replication, the mechanisms of TSE pathogenesis, the epidemiology and natural history of TSEs, and the physiologic function of normal prion protein.

**COMMITTEE ON TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES:
ASSESSMENT OF RELEVANT SCIENCE**

Richard T. Johnson, Chair, Distinguished Service Professor of Neurology, Microbiology, and Neuroscience, Johns Hopkins University School of Medicine
Harvey J. Alter, Chief of the Infectious Diseases Section and Associate Director for Research, Department of Transfusion Medicine, National Institutes of Health

Dean O. Cliver, Professor of Food Safety, Department of Population Health and Reproduction, School of Veterinary Medicine, University of California, Davis

Roger Y. Dodd, Executive Director for Biomedical Safety, American Red Cross Holland Laboratory

Frederick A. Murphy, Professor and Dean Emeritus, Department of Pathology, Microbiology, and Immunology, School of Veterinary Medicine, University of California, Davis

Michael B.A. Oldstone, Professor, Department of Neuropharmacology, Division of Virology, The Scripps Research Institute

David Relman, Associate Professor of Medicine and of Microbiology and Immunology, Stanford University

Raymond P. Roos, Marjorie and Robert E. Straus Professor in Neurological Science, and Chairman, Department of Neurology, University of Chicago Medical Center

David M. Taylor, SEDECON 2000 and retired Principal Research Scientist, Neuropathogenesis Unit, Institute for Animal Health, Edinburgh

Reed B. Wickner, Chief, Laboratory of Biochemistry and Genetics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

Robert G. Will, Professor of Neurology, University of Edinburgh; Director, National Creutzfeldt-Jakob Disease Surveillance Unit; and Consultant Neurologist and Part-Time Senior Lecturer, Department of Neurosciences, Western General Hospital, Edinburgh

Consultants

Adriano Aguzzi, Professor and Associate Dean for Research, Department of Pathology, Institute of Neuropathology, Institute of Neuropathology, University Hospital at Zurich

David M. Asher, Chief, Laboratory of Bacterial, Parasitic, and Unconventional Agents, Division of Emerging and Transfusion Transmitted Diseases, Office of Blood Research and Review, Center for Biologics Research and Evaluation, Food and Drug Administration

Pierluigi Gambetti, Professor and Director, Division of Neuropathology, Case Western Reserve University, and Director, National Prion Disease Pathology Surveillance Center

David A. Harris, Professor, Department of Cell Biology and Physiology, Washington University School of Medicine

Stanley B. Prusiner, Director, Institute for Neurodegenerative Diseases, and Professor of Neurology, University of California, San Francisco

Elizabeth S. Williams, Professor, Department of Veterinary Science, University of Wyoming

Project Staff

Rick Erdtmann, Study Director

Laura B. Sivitz, Research Associate

Reine Y. Homawoo, Project Assistant

Karen Kazmerzak, Research Associate

Next committee meeting:

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The National Academies
500 Fifth Street, N.W.
Washington D.C. 20001

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Contact:

Laura Sivitz, Research Associate
202/334-3826 or Lsivitz@nas.edu

Advancing Prion Science: Guidance for the National Prion Research Program is available for sale from the National Academies Press, 500 Fifth St. NW, Washington, DC 20001; call (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area), or visit the NAP's on-line bookstore at www.nap.edu. For more information about the Institute of Medicine, visit the IOM home page at www.iom.edu.

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