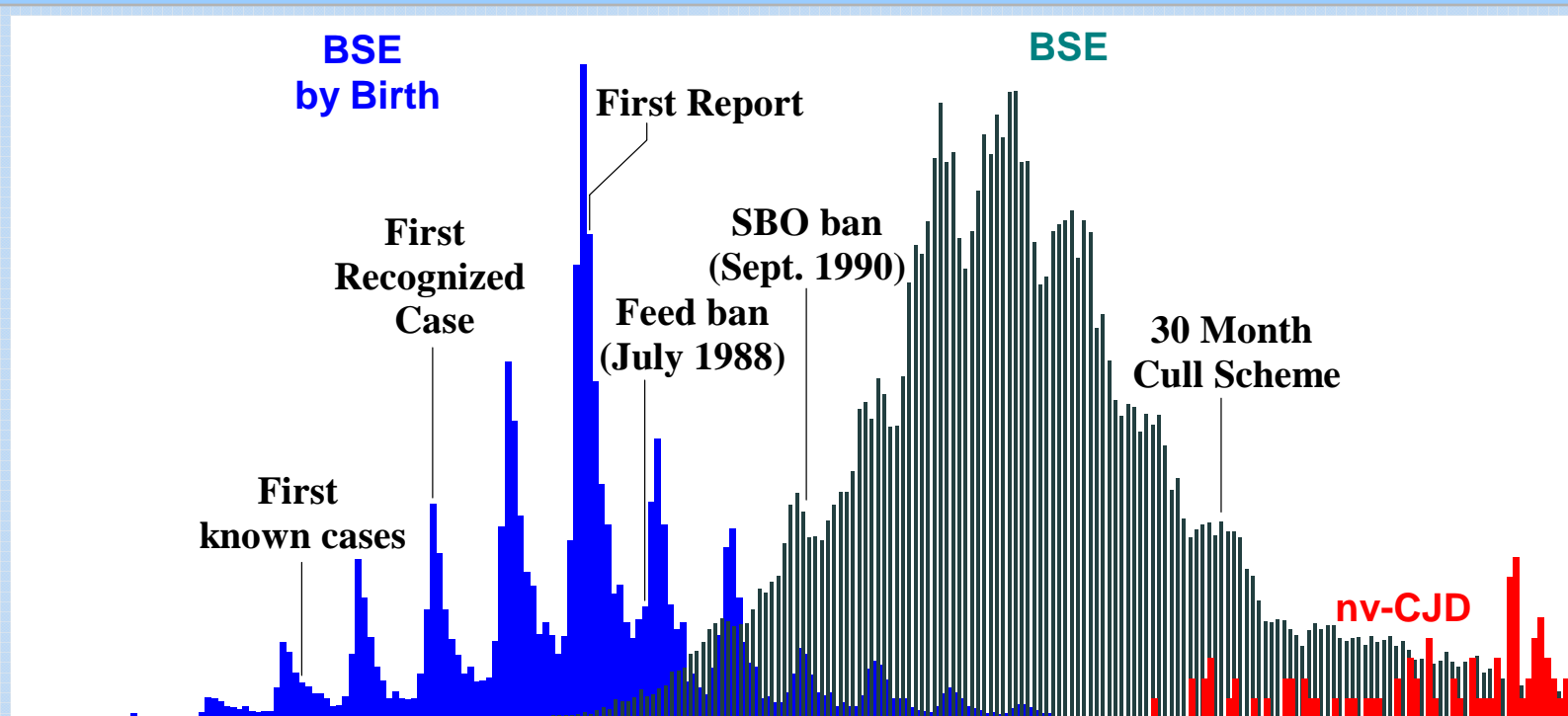


Patient Safety 2010

London, February 4, 2010



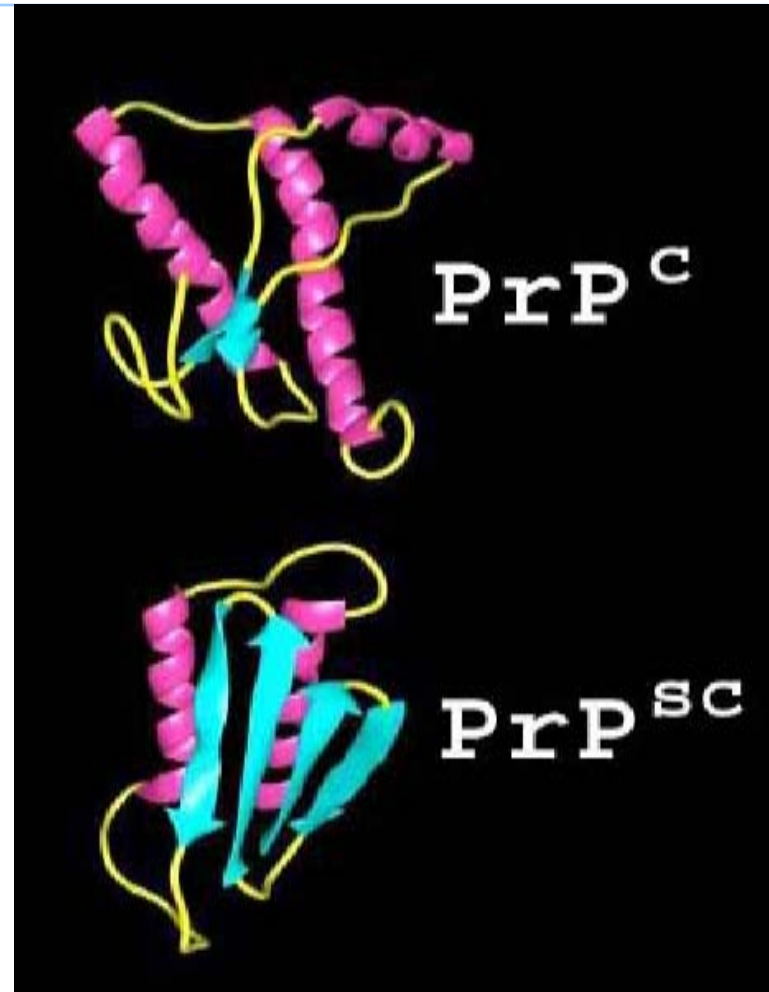
vCJD: An Ongoing Threat to Public Health and its Management

by Robert G. Rohwer, Ph.D.

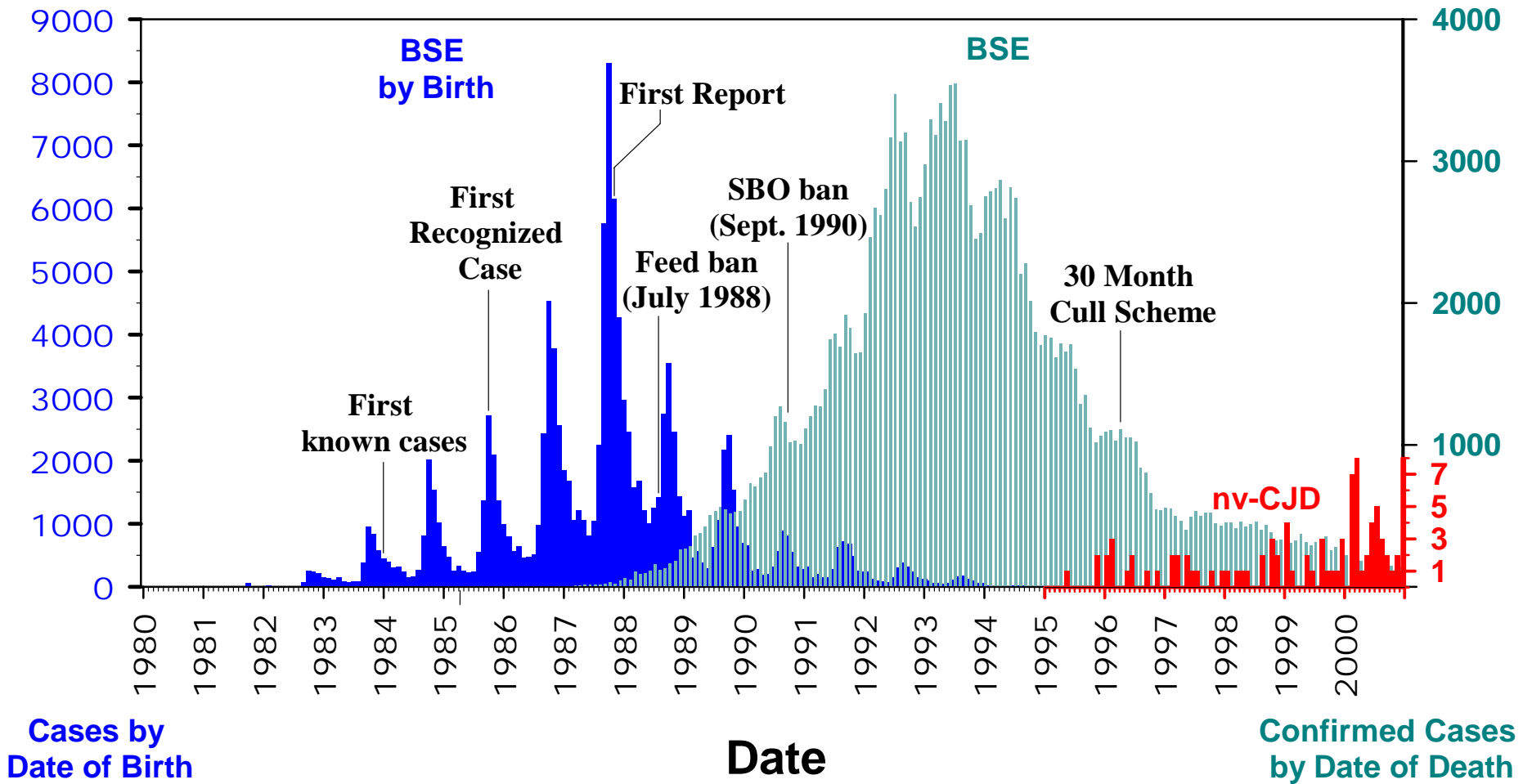
VA Medical Center
University of Maryland
Baltimore, MD

Prions and TSEs

- **Prion proteins** are present in every human brain
- Their normal function is unknown
- If they misfold they cause **prion diseases**.
- They are also called *Transmissible Spongiform Encephalopathies* or **TSEs**



The BSE Epidemic



Animal Models Predict Additional vCJD infections

Case Report

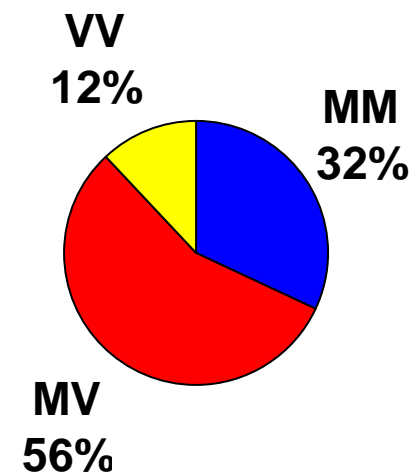
Variant CJD in an individual heterozygous for *PRNP* codon 129

Diego Kaski, Simon Mead, Harpreet Hyare, Sarah Cooper, Ravi Jampara, James Overell, Richard Knight, John Collinge, Peter Rudge

Lancet 2009; 374: 2128

- The prion gene has two major forms, M and V
- A person is either MM, MV or VV
- Only humans with MM have developed vCJD
- Mice and sheep have this polymorphism
- It can have little effect on susceptibility
- It has large effects on incubation time

Distribution of Codon 129 Polymorphism in Caucasians



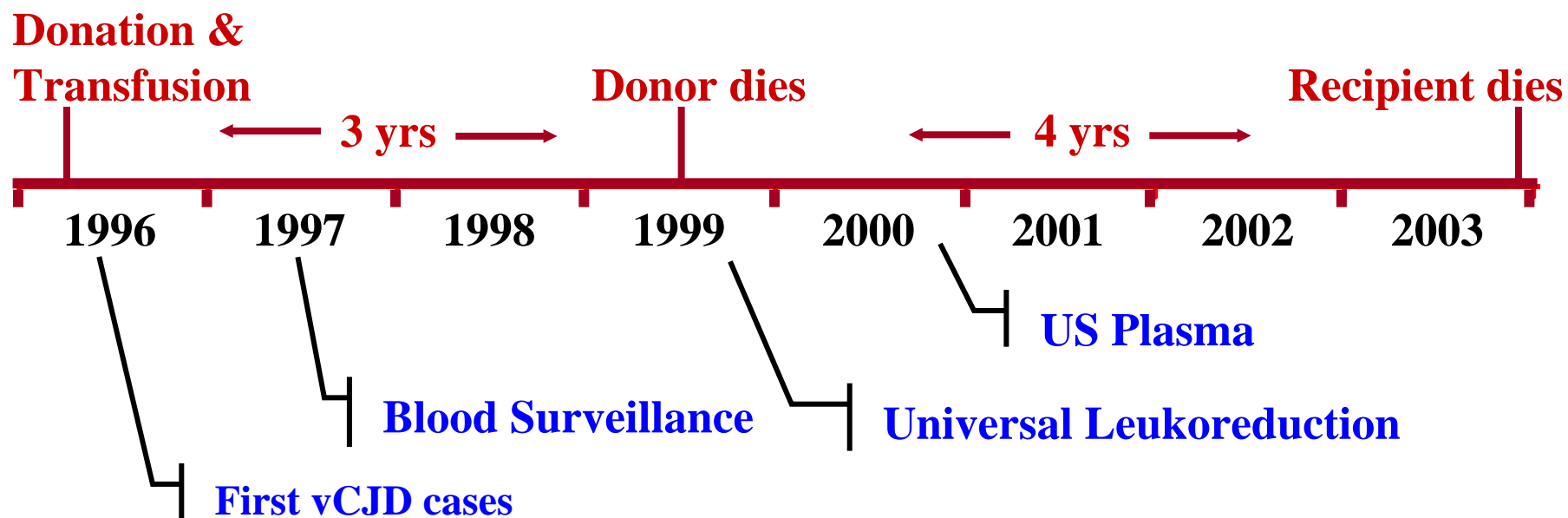
Prevalence of vCJD incubating cases

Prevalence of lymphoreticular prion protein accumulation in UK tissue samples.

David A Hilton, Azra C Ghani, Lisa Conyers, Philip Edwards, Linda McCardle, Diane Ritchie, Mark Penney, Doha Hegazy and James W Ironside J Pathol 2004; 202:

- **Screen appendices and tonsils for PrP^{inf}**
- **Assuming 100% detection efficiency**
 - **Know it is less than 100%**
- **3800 incubating cases x efficiency factor**
- **~380 + vCJD infected blood donors**

Time line for vCJD transfusion transmission



Transfusion Transmissions of vCJD

- **Five cases so far detected**
- **Appears to be highly efficient**
- **At least 40% efficiency in sheep**
 - **Scrapie or BSE**
 - **Symptomatic or incubating donors**

Data from:

Transfusion Medicine Epidemiology Review (TMER), United Kingdom, www.cjd.ed.ac.uk/TMER/TMER.htm

Robert Will, M.D., personal communication. 04-05

Human to human vCJD transmission

- **At least 1000x more efficient than cow to human**
 - **No species barrier**
- **Intravascular route is more efficient than intragastric**
- **Adaptation to more efficient transmission**
- **Increased virulence**

Darwinian Evolution of Prions in Cell Culture

Jiali Li,^{*} Shawn Browning,^{*} Sukhvir P.Mahal, Anja M. Oelschlegel, Charles Weissmann[†]

Department of Infectology, Scripps Florida, 130 Scripps Way, Jupiter, FL 33458, USA.

Control of Pathogens in Blood

- **Sourcing**
 - Defer high risk donors
 - “Geographical deferrals for BSE”
 - North America Plasma
 - **RBC must be obtained locally**

- **Screening**
 - No Antibody and No nucleic acid
 - Technically problematical for TSEs

- **Inactivation**
 - Unrealistic for TSE pathogens

- **Removal**
 - Technically accessible

Blood Transfusion Risk Reduction Measures in the UK

- **Leucodepletion (white blood cell removal) of all Components (July 1998/ Oct 1999)**
- **Deferral of blood donors who were previously transfused after 1980 (April 2004)**
- **Sourcing of plasma from countries unaffected by vCJD**

Advantages of Removal

- **Effective at very low concentrations**
 - **Still active below Limits of Detection**
 - **This could be most of the incubation period**
- **Discrimination of normal vs abnormal PrP is irrelevant**
- **There are no false positive issues**
 - **No notification, counseling, retesting, or trace backs**
 - **or notification, testing, counseling of tracebacks themselves**
 - **or product withdrawals**
- **No alienation of donor population from fear of positive result**
- **Protects against broad spectrum of TSEs (eg. new prion diseases)**

P-Capt™ Prion Reduction Filter

- **Sterile, single use prion-reduction device incorporating a prion-binding affinity resin**
- **Designed for use with leucodepleted Red Cell Concentrate (RCC)**
- **CE Mark approved in Europe**
- **Easily incorporated into blood processing centres and simple to use**
- **Has completed extensive performance and safety testing**



Clinical Experience/Safety Studies

- **Volunteer Clinical Study - 48 persons transfused with P-Capt filtered RCC**
- **Irish Patient Clinical Study - 120 persons transfused with P-Capt filtered RCC**
- **UK Patient Clinical Study Prion-filtered vs Standard Red cells in Surgical and Multi-transfused (PRISM), 540 patient multi-centre study nearing completion**
- **Routine use in selected Irish hospitals**
- **No filter related SAEs**



SaBTO Recommends Prion Filtration

27 October 2009

- *There is now sufficient evidence that this particular filter [P-Capt] reduces infectivity*
- *Filtered red cells should be provided to those born since 1 January 1996, subject to satisfactory completion of the PRISM clinical trial*
- **Currently awaiting a decision by the DoH for adoption of prion filtration in the UK**

SaBTO: Advisory Committee on the Safety of Blood, Tissues and Organs), an independent committee providing advice to Ministers and UK Health Departments

Conclusions

- All recent events warn of a continuing risk from vCJD
- The greatest risk of human to human transmission is from blood use
- Universal adoption of prion removal technologies like the P-Capt filter by MacoPharma is urgently needed to arrest any further spread of the disease by this route

