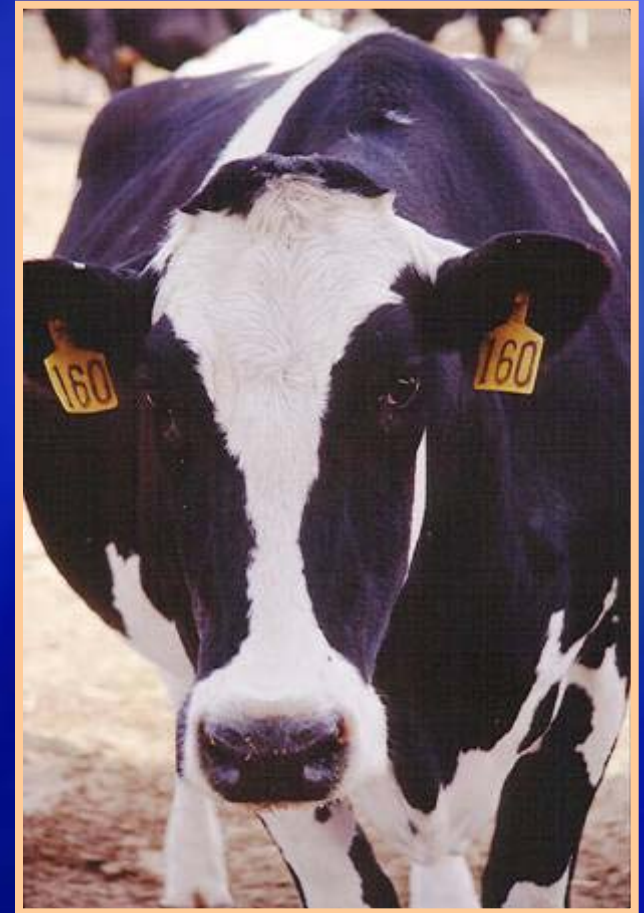


Bovine Spongiform Encephalopathy

Mad Cow Disease

Overview

- Organism
- Economic Impact
- Epidemiology
- Transmission
- Clinical Signs
- Diagnosis and Treatment
- Prevention and Control
- Actions to take



The Organism

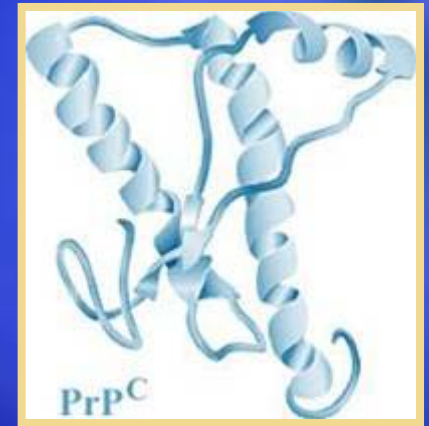
Prion Protein

Prion

- Smaller than smallest known virus
- Not yet completely characterized
- Most widely accepted theory
 - Prion (proteinaceous infectious particles)
- Normal Protein
 - PrPC (C for cellular)
 - Glycoprotein normally found at cell surface inserted in plasma membrane

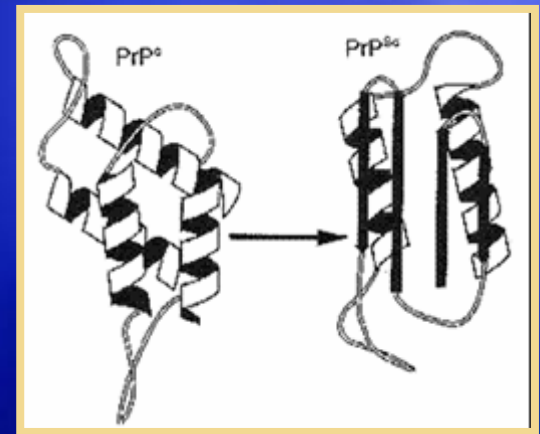
Normal protein

- Secondary structure dominated by alpha helices
 - Probably 3
- Easily soluble
- Easily digested by proteases
- Encoded by gene designated (in humans) PRNP
 - Located on human chromosome 20



Abnormal Protein

- PrP^{Sc} (Sc for scrapie)
 - Same amino acid sequence and primary structure as normal protein
 - Secondary structure dominated by beta conformation



- When PrP^{Sc} comes in contact with PrP^C, it converts it to the abnormal form

Abnormal Protein

- Insoluble in all but strongest solvents
- Highly resistant to digestion by proteases
 - Survives in tissues post-mortem
- Extremely resistant
 - Heat, normal sterilization processes, sunlight
- No detectable immune response in host

Importance

History

- 1986
 - First confirmed case in United Kingdom (UK)
- 1988
 - UK bans meat and bone meal from ruminants in cattle feed
- 1989
 - USDA bans importation of ruminants from countries with BSE

History

- 1993: Peak of BSE in UK
 - 1,000 new cases reported weekly
- 1997: U.S. & Canada banned feeding of ruminant products to ruminants
- 2001: European Union ordered mandatory tests on cattle
 - Older than 30 months destined for slaughter

History

- May 2003:
 - Alberta, Canada
 - BSE diagnosed in a 6-year old Angus beef cow
 - Tracebacks on 40 herds
 - Over 2,000 slaughtered - All negative
 - 1993: Single case in cow imported from UK



Economic Impact

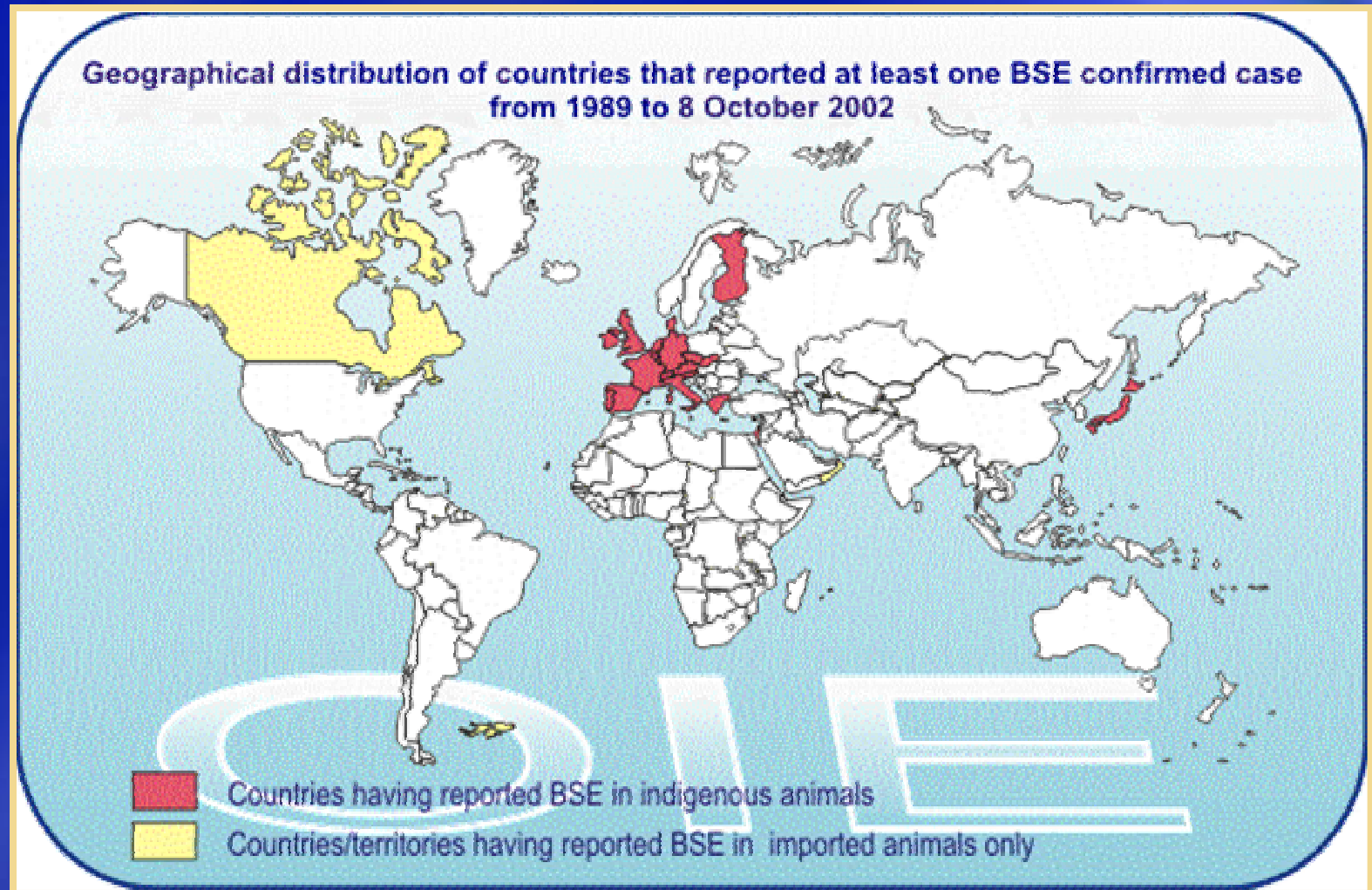
- Single Canadian case
 - 4 month ban
 - Mid-May to mid-September
 - \$2.5 billion
 - Trade losses alone at \$1.5 billion
 - Direct costs
 - Feed, lower prices, reduced sales, disposal of surplus animals
 - Harvest/packaging plants

Economic Impact

- United Kingdom
 - £3.7 billion by end of 2001/02 financial year
 - Compensation alone in 1996/97 was 850 million
 - Prior to 1996, £288 million spent on research, surveillance, compensation
- Very costly, far reaching disease

Epidemiology

Geographic Distribution



Geographic Distribution

- 95% of all BSE cases in U.K.
 - Outside U.K. due to importation or contaminated feed
- U.S. has never identified a case
 - Neither has Australia, New Zealand, South America
- Affected herds
 - 2% morbidity
 - 100% mortality

Transmission

Animal Transmission

- Emergence in cattle
 - Feed contaminated with scrapie or unknown BSE
 - Spontaneous
- Maternal transmission
 - Possible, low risk
 - Retrospective offspring culling
- Currently spread via ingestion of BSE contaminated feed



Human Transmission

- Humans consuming cattle products infected with BSE can develop vCJD
 - Primarily brain and spinal tissue
- Dose required for infection not known
- Genetic susceptibility
 - Methionine homozygous in PrPC



Human Transmission

- Possible modes
 - Transmission from surgical instruments used on tonsils, appendix, or brain tissue
 - Growth hormone injections
 - Vaccines



Human Transmission

- Unlikely modes
 - Blood transmission
 - Consumption of milk and milk products
 - Gelatin products (when manufacturing process is done correctly)



Animals and BSE

Clinical Signs

- Incubation period: Cattle 2-8 years
- Neurological signs initially
 - Apprehension, fear, easily startled, depressed
- Final stages
 - Excitable, hyperreflexia, hypermetria, ataxic muscle fasciculations, tremors

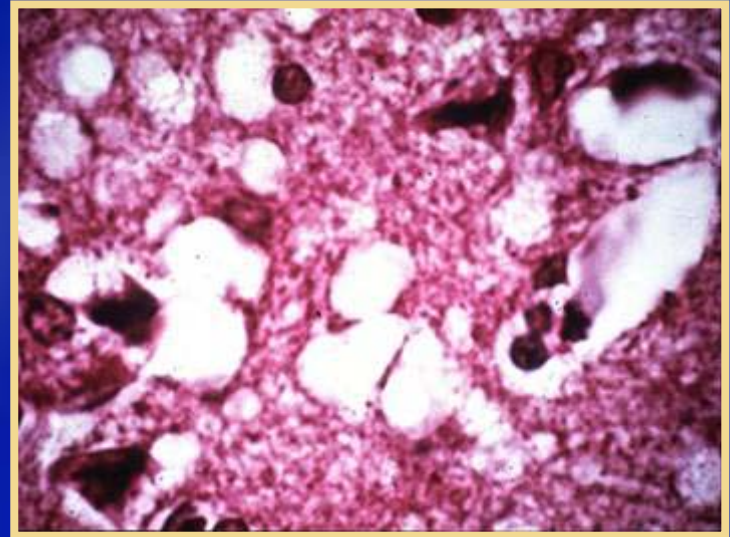
Clinical Signs

- Terminal state
 - Decreased rumination
 - Loss of body weight and condition despite good appetite
- Currently, there is no treatment for BSE



Post Mortem Diagnosis

- Histopathology of brain tissue
 - Spongiform changes in gray matter
- Detection of abnormal prion protein



Sampling

- Before collecting or sending any samples, the proper authorities should be contacted
- Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease

Diagnosis

- Clinically BSE is a slowly progressive, fatal neurologic disease
- Differentials
 - Nervous ketosis, hypomagnesemia, listeriosis, polio, rabies, brain tumor, spinal cord trauma, lead poisoning
- No antemortem testing available
- Brain, stem, medulla, spinal cord

BSE in Humans

Variant Creutzfeldt Jakob Disease (vCJD)

- Consuming BSE contaminated foods
- 1995, UK- First confirmed case
- Incubation period not known
- Mean age at death
 - 28 years old
- Mean duration of infection
 - 14 months

Clinical Signs: vCJD

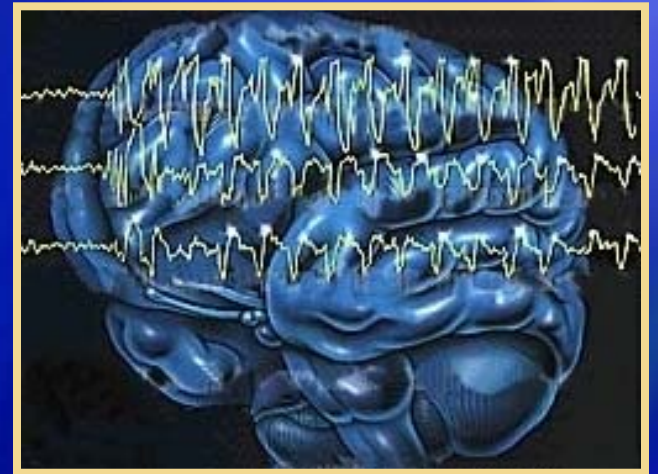
- Initial symptoms
 - Depression and schizophrenia-like psychosis
 - Neurological signs
 - Unsteadiness, difficulty walking, and involuntary muscle movements
- Progression
 - Become completely immobile and mute

Classic Creutzfeldt Jakob Disease (CJD)

- Worldwide 1-2 cases/ million people
- Not caused by eating BSE contaminated food products
- Average age of onset 65 years
- Different forms
 - Spontaneous (85%)
 - Genetic (10-15%)
 - Iatrogenic (<1%)

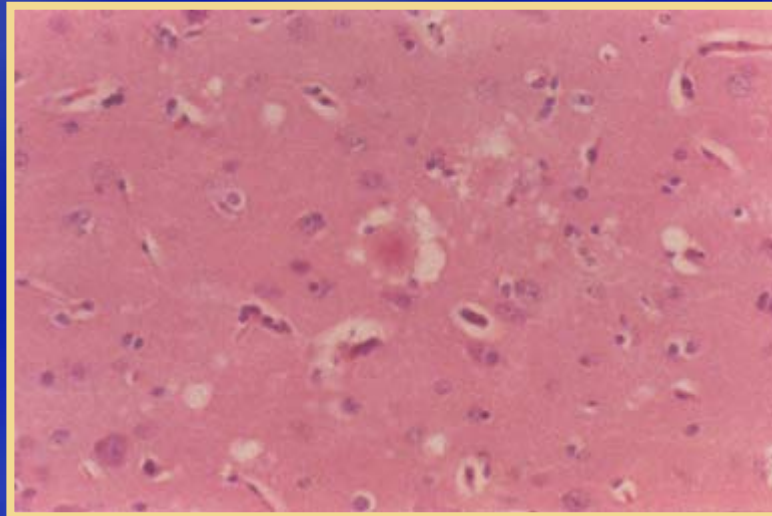
Diagnosis: vCJD

- U.K. criteria for antemortem diagnosis
 - Neuropsychiatric disorder with duration longer than 6 months
 - Specific clinical signs
 - Abnormal EEG
 - Tonsillar biopsy with detection of prion protein



Diagnosis: vCJD

- Post mortem definitive diagnosis
 - Amyloid plaques surrounded by vacuoles
 - Prion protein accumulation in cerebellum
 - Spongiform appearance in gray matter



Treatment: vCJD

- No effective treatment available
 - Experimental drugs under investigation
 - Quinidine
- Symptomatic treatment
- Supportive care

Public Health Significance

- 1995-2003: 132 cases of vCJD reported in U.K.
- No cases of indigenous vCJD in U.S. to date
- Unknown incubation period and consumption
 - Possibly more cases of vCJD in future

Prevention and Control

U.S. Government Precautions

- 1989: Restricted importations
 - On ruminants and ruminant products
 - From countries known to have BSE
 - Eventually included
 - all European nations
- 1997: FDA ban
 - Feeding ruminants most mammalian proteins as food source



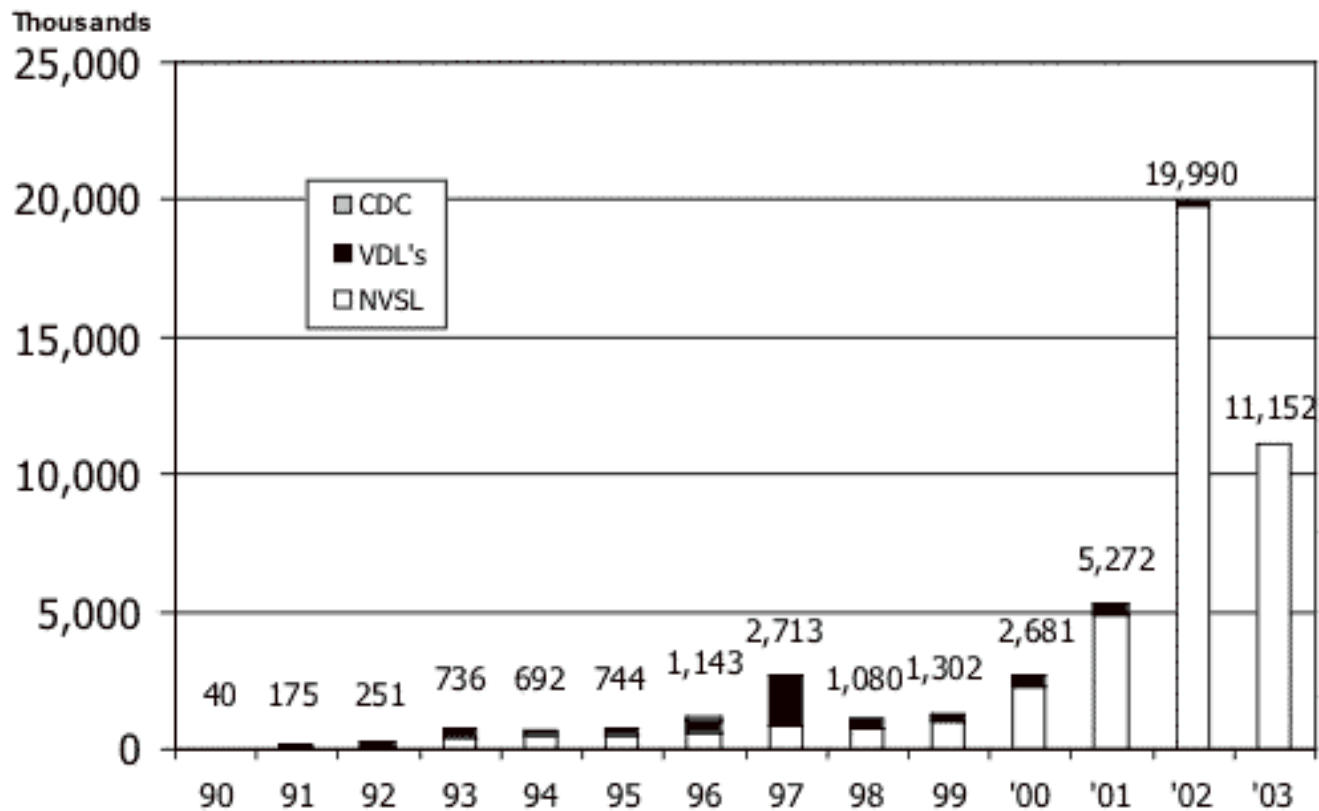
U.S. Government Precautions

- Targeted surveillance of high risk animals
 - Downer cows, older animals, and animals exhibiting signs of neurological disease
- Fiscal year 2002 USDA tested 19,990 animals for BSE
 - Forty one times the number required by the OIE

BSE Surveillance

Yearly totals May 1990 – FY 2003

(through April 30, 2003)



Total since 1990 = 47,944

No evidence of BSE detected

Recommended Actions

- Notify Authorities Immediately of any suspicious cases
- Submit brain, medulla
 - Incinerate the carcass
- Quarantine the premises
- Confirmatory diagnosis
- Depopulation and trace backs
 - Proper disposal of suspect animals



Recommended Actions

- Notification of Authorities
 - Federal:
Area Veterinarian in Charge (AVIC)
www.aphis.usda.gov/vs/area_offices.htm
 - State veterinarian
www.aphis.usda.gov/vs/sregs/official.htm
- Quarantine

Disinfection

- Porous load autoclaving
 - 134-138 °C for 18 minutes
 - Not always effective
- Sodium hypochlorite
 - With 2% available chlorine
- 2-N sodium hydroxide
 - Both on surfaces 1 hour, equipment 8 hours
- Rendering used in Great Britain
- Resistant in tissues, dried organic material, high titer



Vaccination/ Prevention

- No effective treatment or vaccine
- Surveillance program
- Restrictions on blood or plasma donations
 - Persons who have traveled or resided in the U.K. for 3 or more cumulative months from 1980 to 1996
 - FDA Website
www.fda.gov/cber/gdlns/cjdvcjd.pdf

Additional Resources

Internet Resources

- Center for Disease Control and Prevention (CDC) website
 - www.cdc.gov/ncidod/diseases/cjd/cjd_fact_sheet
- World Organization for Animal Health (OIE) website
 - www.oie.int
- Canadian Food Inspection Agency
 - www.inspection.gc.ca/english/anima/heasan/disemala/disemalae

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