

BSE

Pathogenesis, Epidemiology & Risk Assessment

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B. Miguel
Bureau of Animal Diagnostic Laboratories
DAI, DOACS

Hypothesis of TSE?

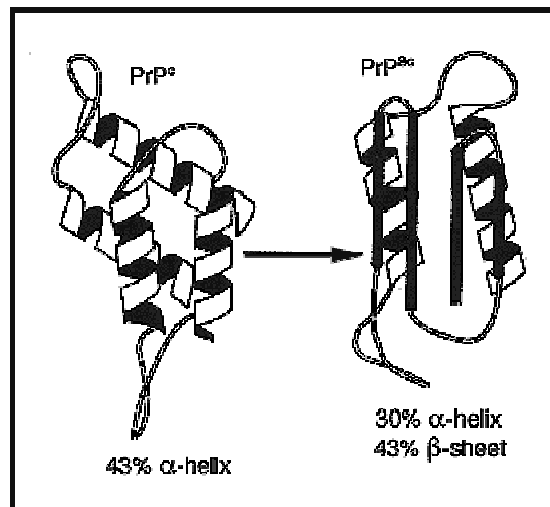
- **Virino**-a particle containing nucleic acid.

Versus

- Misfolded protein; the PrPSc molecule is infectious without the need of genetic material.

Normal versus Abnormal

- | | |
|---------------------------------|---|
| ■ PrP | ■ PrP ^{sc} |
| ■ structure high in alpha-helix | ■ structure high in beta-structure |
| ■ protease susceptible | ■ core residues are <u>protease resistant</u> |
| | ■ forms multimeric aggregates |

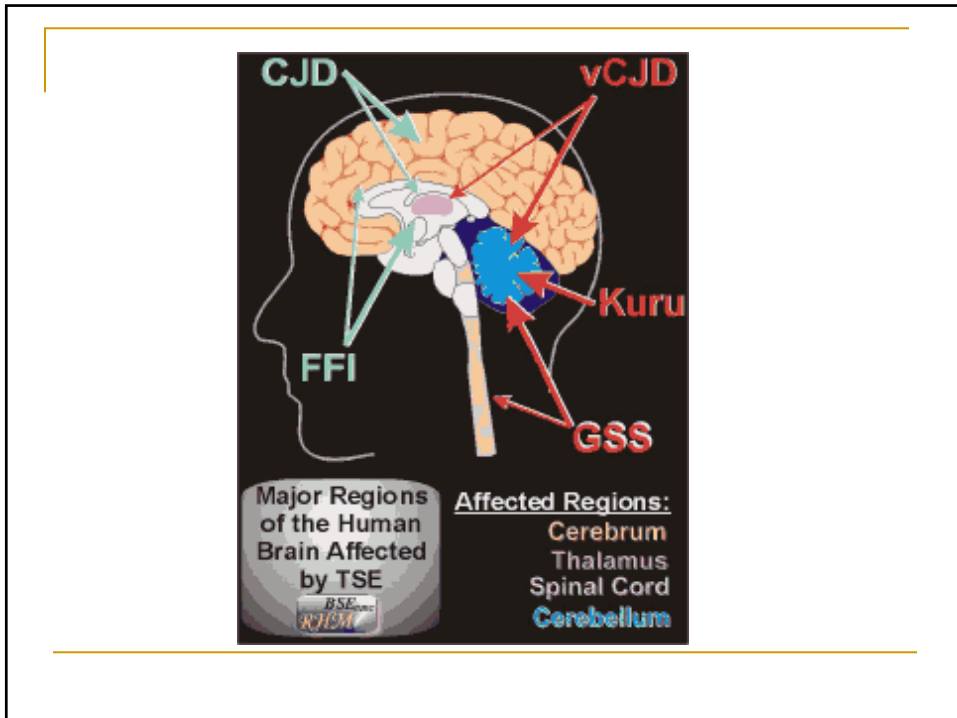


TSE

- Scrapie (sheep and goats)
- Bovine Spongiform Encephalopathy (BSE)
- Chronic Wasting Disease (CWD)
- Transmissible Mink Encephalopathy (TME)
- Feline Spongiform Encephalopathy (FSE, cats)
- Exotic Ungulate Encephalopathy (UEE)
- Large Cat Spongiform Encephalopathy (LCSE)
- Zoo Primate Spongiform Encephalopathy (ZPSE)
- Creutzfeldt-Jakob Disease in human (CJD)
- Kuru
- Fatal familial Insomnia (FFI)
- Gerstmann-Straussler-Scheinker syndrome (GSS)

Human TSE

- Sporadic CJD (sCJD)
- Familial CJD (fCJD)
- vCJD
- Fatal Familial Insomnia (FFI)
- GSS 6 disorders
- Kuru



BSE; Theories how it came to be?

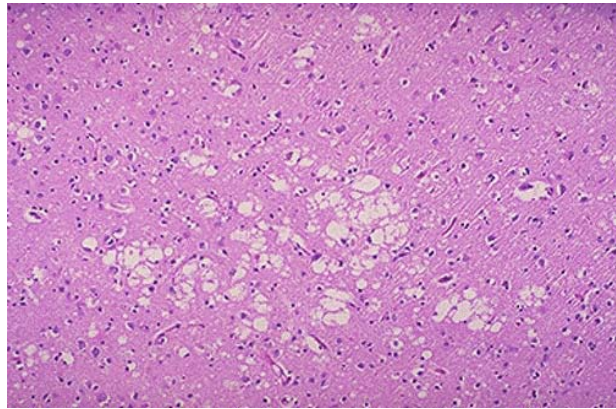
- ❑ BSE /a bovine form of sheep Scrapie
- ❑ BSE arose from a genetic mutation in a single cattle - a single 'spontaneous' misfolding of PrP to PrP^{Sc} caused the disease –

BSE Characteristics

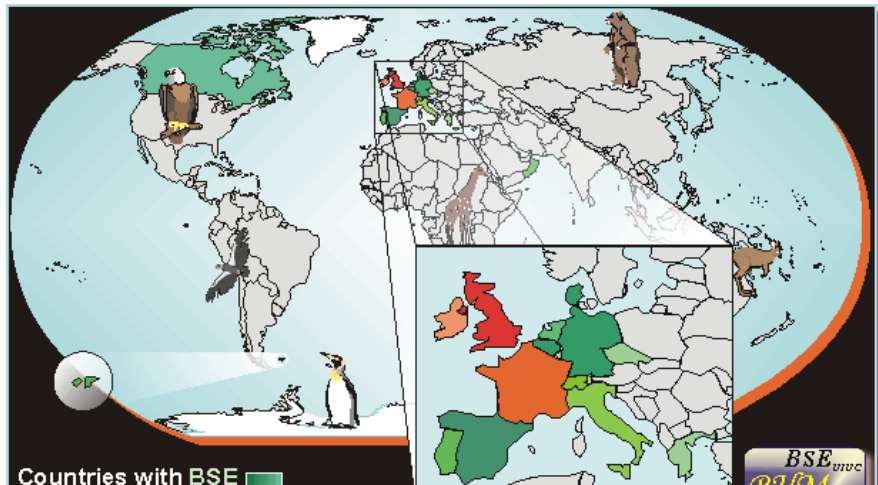
- Many proteins are inactivated or destroyed when offal is processed (rendered) before being used as an animal feed
- The normal PrPC protein is easily destroyed by other proteins (proteases) in the body
- However, the misfolded PrPSc is very stable

BSE/CJD

- Variant Creutzfeldt-Jakob Disease (vCJD)
- The disease is fatal and has been casually linked to the consumption of either BSE meat
- To date vCJD has only been found in the UK, France and Ireland



Countries With vCJD/BSE



The Spread of BSE



What is the greatest human concern relating to BSE?

Incubation time of the disease.

- From the time a cattle contracts the disease until clinical symptoms arise may be several years; the incubation period of the disease.
During this preclinical period the level of infectivity of tissues from cattle is not known.
Several companies and research labs are developing new tests to identify the disease earlier (preferably before clinical signs are manifested) to aid in the

BSE/Risk Infectivity

■ **Highest infectivity**

- brain
- spinal cord
- eye

■ **Medium infectivity**

- spleen
- tonsil
- lymph node
- ileum
- proximal and distal colon
- pituitary gland
- adrenal gland
- cerebrospinal fluid
- placenta

BSE Clinical Symptoms

- **Changes in temperament (nervousness or aggression)**
- **Abnormal posture**
- **Incoordination and difficulty in rising**
- **Decreased milk production**
- **Loss of body conditioning**
- **No change in appetite early in the disease**

Prevention

- **Since the disease is not spread by animal-to-animal contact (horizontally) eradication is possible by:**
 - ① **the destruction of sick animals**
 - ② **Not feeding cattle or other animals offal containing bovine brain**
 - ③ **Careful slaughter and meat processing procedures to ensure that edible products are not contaminated with brain or spinal cord tissue**
 - ④ **Not eating cattle brain**
 - ⑤ **Monitoring or destruction of offspring from affected animals; vertical transmission (from mother to offspring) may occur although with a very low incidence**

Prevention

- **There is no evidence that semen can transmit BSE and thus semen may be imported from countries with BSE**
 - however donors cannot have BSE
 - cannot have parents with BSE
 - must not have sired offspring diagnosed with BSE
 - the semen donor cannot have resided on a farm with BSE
 - the donor has not been feed meat and bone meat with ruminant-derived protein

- **There is some inconclusive evidence that embryos may obtain BSE by placental transfer of PrPSc**
 - hence importation of bovine embryos from countries with BSE and at high risk has been banned

Prevention

- **There is no evidence at this point that human serum or plasma derived from donated blood can transmit BSE.**

- **Several cautionary actions have been taken to ensure that the blood supply remains safe.**
 - **The Red Cross has restricted donations from persons that have visited countries with BSE.**

 - **Several companies are working on tests to determine if blood and blood products contain the transmissible agent that causes BSE.**

Risk Assessment

Risk assessment takes into account a number of factors

- Current disease regional distribution
 - Identification of pathway or practices that could contribute the most to the spread of TSE
 - The amount of potentially dangerous tissues in the human food supply
 - Meat production and consumption patterns
 - Incubation periods and observed vCJD cases
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Risk Assessment

From 1998 to 2001, a risk analysis conducted by Harvard University's School of Public Health

- Noncompliance with the FDA feed ban
 - Rendering of downer cattle
 - Consumption of high risk tissue
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USA Risk Analysis/Actions

- Due to quick and decisive action by the USDA and FDA to restrict imports of animals and products from Great Britain, there have been no confirmed cases of BSE (bovine spongiform encephalopathy) in the US.
- Diligence of government agencies, universities, veterinarians and producers is needed to maintain this status.



USA Today....

1. Work with international experts to develop new protocol utilizing both IHC and the SAF immunoblot.
2. Review our procedures and antibodies for the IHC test.
3. Ensure that sample collection and submission procedures are accurate and followed.
4. Protocol for research must be thoughtful.
5. USDA did not complete prepare paperwork after the original IHCs were completed.
6. Give accurate instructions to ensure that freezing of samples was not done unless absolutely necessary.

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