

NERVOUS SYSTEM (L-4)



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Animal TSE's

- ✦ Bovine Spongiform Encephalopathy (BSE, "mad cow disease")
- ✦ Scrapie (sheep)
- ✦ Chronic wasting disease (elk and deer)
- ✦ Mink Spongiform Encephalopathy
- ✦ Feline Spongiform Encephalopathy

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BOVINE SPONGIFORM ENCEPHALOPATHY

- ✦ mad cow disease, is a chronic, a-febrile, degenerative disease affecting the CNS of cattle.
- ✦ Small % Exhibit Aggressive Behavior "**Mad Cow**"
- ✦ BSE is an invariably fatal disease of domestic cattle, belong to **transmissible spongiform encephalopathies (TSE) or PRION diseases**
- ✦ These diseases are defined by the pathological **accumulation of a host-encoded protein (designated PrP^{C/BSE}), principally in the CNS but also in lympho-reticular tissues**
- ✦ PrP, is the only detectable macromolecule associated with infectivity.
- ✦ Japan banned the domestic use of ruminant protein for ruminant feed on 18 September 2001



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BOVINE SPONGIFORM ENCEPHALOPATHY

Aetiology and Epidemiology

- ✦ First case of BSE – around April **1985-86** in Surrey, **UK**
- ✦ The initial epidemiological studies – feed borne infection (meat-and-bone meal)
- ✦ Reported from almost all Europe
- ✦ Transmitted – **Parenteral and oral exposure to brain tissue**
- ✦ Experimentally transmissible to cattle, pigs, sheep, goats, mice, etc.
- ✦ **Offspring at high risk – true maternal transmission?**
- ✦ No horizontal transmission
- ✦ **Incubation** period is months to years (**2 to 8 years**)
- ✦ Clinical disease in **adult cattle – 4-5 years of age**
- ✦ Occurrence of new variant Creutzfeldt-Jakob disease (CJD) suggests zoonotic potential via oral exposure.
- ✦ Sources of human infection, CNS of naturally occurring clinically affected cases.

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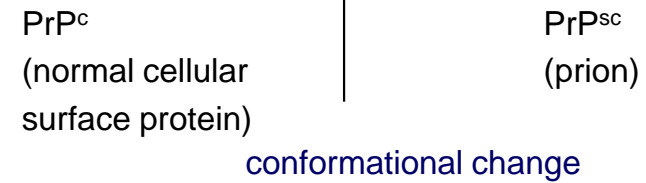
Prusiner named this protein: **PRION** from:

Proteinaceous Infectious Only



Cause of BSE

Prion theory: "PROteinaceous INfectious particle or particle" (1982)



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Rendered Protein Ingredients:

Animals unfit for human consumption such as:

- ❖ Sick cows
- ❖ Sick pigs
- ❖ Sick turkeys, chicken and ducks
- ❖ Horses
- ❖ Sick catfish, salmon and shrimp
- ❖ Cats and dogs
- ❖ Zoo animals
- ❖ Road kill



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More ingredients:

- ❖ Frying oil from restaurants
- ❖ Brains, spinal cords, feathers, hooves, skins, hair, fur, whiskers, bones, teeth, etc. remaining from slaughterhouses
- ❖ Sewage sludge
- ❖ Manure
- ❖ Sawdust/wood scraps
- ❖ Newspaper
- ❖ Cement dust
- ❖ Maggot infested grains



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Worker Hazardous Exposures

- ✦ Dangerous chemicals such as hydrogen sulfate, potassium permanganate, chlorine gas, sodium hypochlorite, lime, formaldehyde, NaOH, acetic acid and phosphoric acid.
- ✦ Extreme Heat
 - ▣ When heat in process was lowered in response to worker safety issues, process does not sufficiently remove contaminants: Salmonella, E. coli, infectious prions, pesticides, pharmaceuticals and hormones. These contaminants not only pose a problem for the animals ingesting the food but also for the workers handling the product.
- ✦ Aerosolized fat mist that sprays out of the vats coats the walls and floor of the plant, making all surrounding surfaces very slippery and creating an extreme fire danger.

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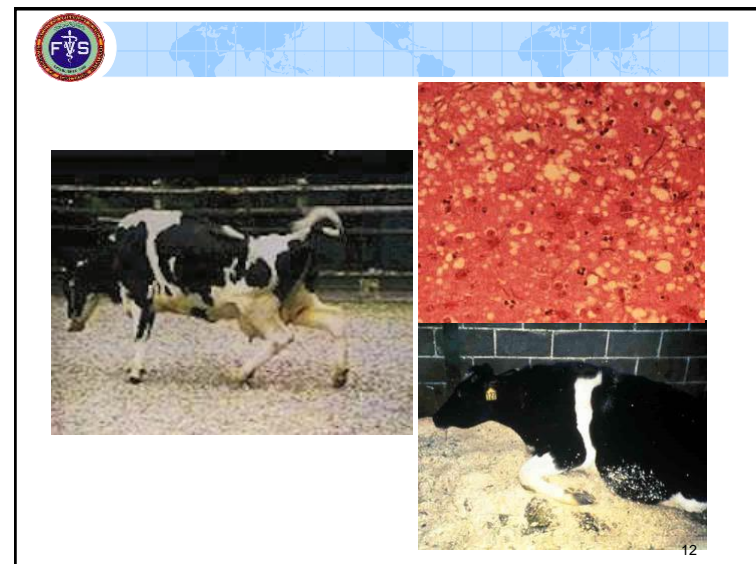
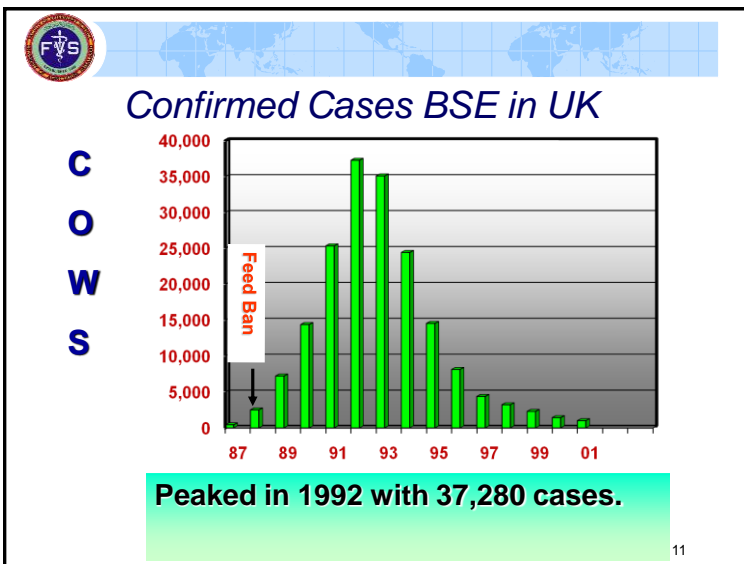
Recycling?


The rendering industry defends their work as a form of “recycling”

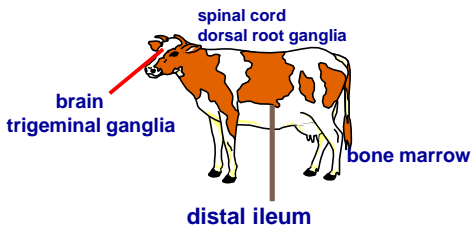
- ✦ **1.3 million tons in the U.K. in 1988**
- ✦ **15 million tons in the U.S. in 1992**

This is waste that would have otherwise gone into landfill.


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 **Distribution of Infectivity**




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 **1988; the year of action**

- ⊕ Minimal risk to humans
- ⊕ Slaughter all infected cattle
- ⊕ Do not eat clinically sick animals
- ⊕ As the disease was simply scrapie, and scrapie did not spread to humans
- ⊕ No risk of zoonosis, continue to eat bovine brain
- ⊕ Half the value of a non-sick animal was given in compensation

 **1989, the year of the specified offals ban**


- ⊕ The Spongiform Encephalopathy Advisory Committee, immediately recommended that
 - ❑ Specific offals (brain, spleen, thymus, tonsil, gut) should be discarded
 - ❑ All clinically ill cattle should be destroyed by incineration or burial.
- ⊕ Experimental transmission to
 - ❑ mice in the laboratory
 - ❑ various zoo animals through the eating of the same feed.

 **1990; the year of the media hype**

- ⊕ The CJD surveillance unit was set up in Edinburgh to find out if BSE was giving rise to extra cases of CJD.
- ⊕ **Minister's daughter** refused beef burger in front of the press
- ⊕ 300 cases per week.
- ⊕ Full value compensation stepped up
- ⊕ The German Government stopped British beef

 **1991; the year of refusals**

- ✦ UK experts were sent to convince that BSE was not a risk.
- ✦ **Harash Narang** was told to stop carrying on his research into BSE and its risk to humans.
- ✦ A case appeared in a cow that was born after the feed ban
- ✦ **Fears of spread** of BSE across Europe because export of infected animals
- ✦ Directives on how to handle BSE infected carcasses


 **BOVINE SPONGIFORM ENCEPHALOPATHY** 18

Aetiology and Epidemiology


- ✦ Worldwide there have been more than 170,000 cases since the disease was first diagnosed in 1985 or 1986 in Great Britain.


Pathophysiology

- ✦ Slowly developing disease
- ✦ Rarely acute and then deteriorate rapidly
- ✦ Signs – variable
- ✦ Reluctant to enter the milking parlor – or may kick vigorously during milking
- ✦ In dry cows — pelvic limb **in-coordination and weakness**

 **BOVINE SPONGIFORM ENCEPHALOPATHY** 19

- ✦ Neurological signs predominate throughout the clinical course and may include
 - ▣ Related with altered mental status and behavior,
 - ▣ abnormalities of posture and movement, and aberrant sensation,
 - ▣ **Most common — apprehension, pelvic limb ataxia, and hyperesthesia to touch and sound**
- ✦ **Death** occur from **2 weeks to 6 months** after clinical signs are seen.
- ✦ Affected cows sometimes stand with low head carriage, the neck extended and the ears directed caudally
- ✦ **Abnormalities of gait – swaying (wobbling) of the pelvic quarters**
- ✦ **Generalized weakness — falling and recumbency**
- ✦ **Pruritis**, seen in scrapie, occurs also but is not usually a prominent sign.


 **BOVINE SPONGIFORM ENCEPHALOPATHY** 20




Cattle affected by BSE show changes in temperament (e.g., nervousness or aggression), abnormal posture, and incoordination.

APHIS photos by Dr. Art Davis


http://www.aphis.usda.gov/lpa/issues/bse/bse_photogallery.html

 **Prion protein is indestructible**
by heat up to 1000° F (350° C)
Hot enough to melt lead.

In 1986, 4.5 million cows were incinerated in the U.K. after the discovery of BSE. The ashes, stored in underground concrete containers, were retested again in 1998 and found to still be infected with active prions.




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 **BOVINE SPONGIFORM ENCEPHALOPATHY** 22


Diagnosis

- ✦ There are no gross post-mortem changes.
- ✦ For details refer to *OIE Manual*.
- ✦ Injection to mice
- ✦ The specific pattern of neuropathology
- ✦ Morphological features of **spongiform encephalopathy**
- ✦ Electron microscopy — characteristic fibrils, termed **scrapie-associated fibrils (SAF)**, which are composed largely of PrP^{Sc}
- ✦ PrP^{Sc} detection — immunohistochemistry, Western blotting and other immunoassays
- ✦ Histologic changes in the CNS, bilateral usually symmetric, **vacuolation of gray matter neuropil** (spongiosis) and **neurons**, similar to the lesions seen in scrapie.

 **BOVINE SPONGIFORM ENCEPHALOPATHY** 23

Differential Diagnosis

- ✦ Rabies
- ✦ Listeriosis
- ✦ Nervous ketosis
- ✦ Milk fever
- ✦ Grass tetany
- ✦ Lead poisoning and
- ✦ Other toxicities or etiological agents affecting the nervous or musculoskeletal system of adult cattle



Brain. The red box indicates the portion of the brain that must be obtained for the diagnosis of BSE and other spongiform encephalopathies such as scrapie and chronic wasting disease

 **SCRAPIE**
(Ovine Spongiform Encephalopathy)

- ✦ A naturally occurring progressive, fatal, infectious neurodegenerative disease of **sheep** and **goats** characterized by vacuolar or spongy changes in CNS
- ✦ It is the first TSE or prion disease of mammals to be recognized
- ✦ Recognized more than 250 years ago and Started from Spain

Aetiology and Epidemiology

- ✦ Endemic in many European countries
- ✦ However, Australia and New Zealand have maintained freedom from the disease through rigorous preventive policies.
- ✦ Caused by Prion.
- ✦ Clinical disease occurs in adult sheep (2-5 years old)
- ✦ Infected animals — even without clinical disease is source of spread.
- ✦ Most breeds are affected,

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SCRAPIE
(Ovine Spongiform Encephalopathy)

Aetiology and Epidemiology

- ✦ May spread from **ewe to lamb**
- ✦ Infection can also pass to unrelated sheep or goats, especially when parturition occurs in confined areas. **Foetal membranes are thought to be a source of infection**
- ✦ The clinical disease only develops if the infection enters the CNS.

Pathophysiology

- ✦ Clinical signs usually start subtle (secretly)
- ✦ Sheep may **lead or trail the rest of the flock**
- ✦ Sheep may have a **star gazing** appearance
- ✦ May be ataxia or in-coordination of gait.

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SCRAPIE
(Ovine Spongiform Encephalopathy)

- ✦ Either the pruritis or the ataxia usually emerges to dominate the clinical course
 - ❖ Compulsive **rubbing** or **scraping** against fixed objects,
 - ❖ **Nibbling**, can often be elicited by palpation of the lumbar region
 - ❖ **Loss of wool**, particularly over the lateral thorax, flanks and hindquarters
 - ❖ self-inflicted skin lesions.
 - ❖ Stumbling and falling occur
 - ❖ These signs progress to weakness and recumbency.

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SCRAPIE
(Ovine Spongiform Encephalopathy)


- ✦ Other neurological signs may include
 - ❖ teeth grinding (**bruxism**),
 - ❖ an abnormally low carriage of the head and ears,
 - ❖ a fine tremor (involuntary shaking),
 - ❖ seizures (epileptic fit), and
 - ❖ Blindness
- ✦ May be hyperesthesia to sound, movement or touch
- ✦ Polydipsia and polyuria may be evident
- ✦ Fatal outcome

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SCRAPIE
(Ovine Spongiform Encephalopathy)





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 **SCRAPIE**
(Ovine Spongiform Encephalopathy)

Diagnosis

- ✦ A modified form (prion protein Sc for scrapie– PrP^{Sc}) of a host-coded, highly conserved, membrane glycoprotein (PrP^c · c - cell), of unknown function, is the only macromolecular constituent of the infectious agent identified.
- ✦ Transmission from infected tissues, usually to **laboratory rodents by injection, is the only available means of detection of infectivity and requires incubation periods of 1-2 years.**
- ✦ Pathological changes.
- ✦ There are no specific gross pathological changes seen in scrapie.

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 **SCRAPIE**
(Ovine Spongiform Encephalopathy)

- ✦ The histological lesions are confined to the CNS and most reports of the changes have described those occurring in the brain.
 - ▣ Neurodegenerative
 - ▣ Vacuolation in neuronal processes produces the distinctive appearance of spongiform change in the neuropil of grey matter.
 - ▣ There may also be neuronal loss, gliosis and amyloidosis.
 - ▣ Typically, the lesions have a bilaterally symmetrical distribution.
 - ▣ Lesions are usually most apparent in the brain stem.
- ✦ Immunohistochemistry
- ✦ immunoblotting

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 **Suggested Resources for Further Information:**

- ✦ NDSU Extension BSE Frequently Asked Questions:
www.ext.nodak.edu/pubs/ansci/beef/bse-faq.pdf
- ✦ NCBA's BSE Web Site: 
www.bseinfo.org 
- ✦ USDA/APHIS Veterinary Services: 
www.aphis.usda.gov/ia/issues/bse/bse.html 
- ✦ Centers for Disease Control and Prevention: 
www.cdc.gov/ncidod/diseases/cjd/cjd.htm 
- ✦ Food and Drug Administration: 
www.fda.gov/cvm/index/bse/bsetoc.html 
- ✦ Council for Agricultural Science and Technology: 
www.cast-science.org/cast/src/cast_top.htm
- ✦ United Kingdom Ministry of Agriculture Fisheries and Food 
[%20http://www.defra.gov.uk/animalh/bse/index.html](http://www.defra.gov.uk/animalh/bse/index.html)

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 **HAVE A GOOD TIME!**



THE END

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