

S
l
i
d
e
1

Bovine Spongiform Encephalopathy

Mad Cow Disease



Last Updated: July 10, 2007

Bovine spongiform encephalopathy is also commonly referred to as Mad Cow Disease. This is a neurologic disease causing a generalized appearance of microscopic holes in the brain that resemble a sponge. Thus was born the term spongiform encephalopathy (encephalon meaning "brain" and pathos meaning "disease of").

S
l
i
d
e
2

Overview

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



Center for Food Security and Public Health
Iowa State University - 2007

In today's presentation we will cover information regarding the organism that causes bovine spongiform encephalopathy (BSE) and its epidemiology. We will also talk about the economic impact the disease has had in Canada and the UK. Additionally, we will talk about how it is transmitted, the species it affects, human repercussions, clinical and necropsy signs seen, as well as diagnosis and treatment of the disease. Finally, we will address prevention and control measures for the disease put in place by the USDA and FDA and actions to take if BSE is suspected.

S
l
i
d
e
3

The Organism

Prion Protein



S
l
i
d
e
4

Prion

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

Center for Food Security and Public Health
Iowa State University - 2007

Prions are smaller than the smallest known virus and have not yet been completely characterized. The most widely accepted theory is that prions are mutated proteins, although not all scientists accept they are the cause of disease. Professor Stanley Prusiner, the Nobel prize winning scientist who first proposed that prion proteins could cause disease, says that today "a wealth of experimental and clinical data" proves his ideas were right. The idea of a protein-only infectious agent was first proposed by Griffiths in 1967. However, it was only after the co purification of the prion protein with hamster scrapie infectivity that Prusiner was able to distinguish it from a virus. The normal protein is designated as PrP^C the C stands for cellular. The glycoprotein is normally found at the cell surface and is inserted in the plasma membrane.

S
l
i
d
e
5

Normal protein

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



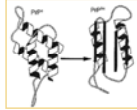
Center for Food Security and Public Health
Iowa State University - 2007

The secondary structure of the normal protein is dominated by **alpha** helices. There are likely three of these structures. The normal protein is easily soluble and digested by proteases. This gene in humans is designated PRNP and located on our chromosome 20. Image from www.prionics.ch, shows normal cellular prion protein.

S
l
i
d
e
6

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} contacts PrP^C
 - Converts it to the abnormal form



Center for Food Security and Public Health
Iowa State University - 2007

The abnormal protein is designated as PrP^{Sc}, the Sc stands for scrapie, a spongiform encephalopathy in sheep. This protein has the same amino acid sequence as the normal protein and the primary structures are identical. The secondary structure is dominated by a **beta** conformation. When the abnormal protein comes in contact with the normal protein (PrP^C) it converts the normal protein to its abnormal form. Diagram depicts normal prion on left, abnormal on right.

S
l
i
d
e
7

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

Center for Food Security and Public Health
Iowa State University - 2007

The abnormal protein is insoluble in all but the strongest solvents and is highly resistant to digestion by proteases. It survives in tissues post-mortem and is not destroyed by various rendering processes. The abnormal form of the protein is extremely resistant to heat, normal sterilization processes and sunlight. It is also very resistant to most disinfectants and is stable at a wide range of pH. The abnormal protein also does not evoke a detectable immune or inflammatory response in its host so the body does not react to it as an invader.

S
l
i
d
e
8

Importance



S
l
i
d
e
9

History

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

Center for Food Security and Public Health
Iowa State University - 2007

The first confirmed case of BSE occurred in 1986 in the United Kingdom. Following that discovery, in 1988 the UK banned meat and bone meal products rendered from ruminants from inclusion into cattle feed. In 1989, the United States Department of Agriculture (USDA) banned the importation of live ruminants and most ruminant products from countries that were known to have BSE. Major efforts were made to stop the spread of this disease in the UK and continue today. Roughly 5.8 million cattle in the U.K. over thirty months of age were slaughtered up to June 23, 2003 in continued efforts to stop the spread this devastating disease.

S
l
i
d
e
10

History

- 1993
 - Peak of BSE in UK
 - 1,000 new cases reported weekly
- 1997
 - US and Canada ban feeding of ruminant products to ruminants
 - US importation ban extended to all of Europe
- 2001, European Union ordered mandatory tests on cattle
 - Older than 30 months destined for slaughter

Center for Food Security and Public Health
Iowa State University - 2007

The peak incidence of BSE in the UK occurred in January 1993, with more than a 1,000 cases being reported weekly. Since then, the number of new cases has been decreasing at a steady pace (number of cases reported in 1993 was 35,000; in 2006 the case number had decreased to 114 – much lower). In 1997, Canada and the FDA of the United States instituted a ban on feeding ruminant meat, bone meal, and other ruminant proteins, back to ruminants. Additionally in 1997, the U.S. extended its ruminant import ban to all of Europe regardless of BSE status. In 2001, the European Union ordered mandatory testing to be done on cattle older than 30 months of age that are destined for slaughter. Information on UK case numbers obtained: http://www.oie.int/eng/info/en_esbru.htm

S
1
i
d
e
1
1

History: Canada

- 1993
 - Cow imported from UK
- 2003, Alberta
 - May, 6 yr old Angus beef cow
 - Over 2,500 slaughtered, all negative
 - Dec, 6½ yr old Holstein living in U.S.
- 2004, 2005: 1 case each year
- 2006: 5 cases
- 2007: 2 cases as of May 2007



Center for Food Security and Public Health
Iowa State University - 2007

Canada's first case of BSE was in 1993 in a single cow imported from the U.K. In 2003, Alberta Canada had 2 cases of BSE diagnosed in indigenous cattle, the first occurring in May 20, 2003 when it was discovered in a 6-year old Angus beef cow. In January, this animal was recumbent and unable to rise. The owner opted for slaughter for personal use of the meat. It was condemned due to pneumonia and never entered the human food chain. The lag time for diagnosis was due to other priorities, as BSE was not a concern prior. Tracebacks were done on 40 herds and 2,700 cattle were slaughtered, all of which were over 24 months of age and all were found to be BSE negative. In December 2003, a 6 ½ year old Holstein cow tested positive in Washington State in the US. It was later discovered that this cow, along with her cohorts, were shipped from Alberta, Canada. See next slide for more details. In January 2005, an 8 year old Holstein and a 6 year old beef cow were found to be BSE positive. None of their carcasses entered the human food chain. All birth cohorts and offspring were slaughtered and tested; all negative. Canada continues to diagnose BSE – 2004 1 case, 2005 1 case, 2006 5 cases, and 2007 2 cases as of May 2007. Status of Canadian cases can be found at: http://www.oie.int/eng/info/en_esbmonde.htm

S
1
i
d
e
1
2

History: U.S.

- December 2003, Washington State
 - Dairy cow
 - 6½ years old
 - Imported from Canada
 - Confirmed by DNA tests
 - Complications following calving
 - Sent to slaughter
 - Brain tissue sent to NVSL-per FSIS protocol
 - Presumptive positive
 - Definitively positive by UK lab

Center for Food Security and Public Health
Iowa State University - 2007

On December 23, 2003, the U.S. announced the discovery of its first case of BSE. Diagnosis was confirmed by an UK world reference diagnostic laboratory on December 25, 2003. The case involved a 6-1/2 year old dairy cow sent to slaughter on December 9, following complications following calving ("downer"). The cow was identified prior to slaughter as a BSE suspect for testing. [Note: In 2003, U.S. surveillance testing for BSE included "downer" cattle, adult cattle exhibiting neurological signs, rabies-negative cattle and cattle that die on the farm.] Brain tissue samples were forwarded to the USDA National Veterinary Services Laboratory for testing. Upon determining a presumptive positive diagnosis, samples were hand carried to the world reference laboratory in the UK. Confirmatory diagnosis of BSE was reported on December 25, 2003. DNA testing by USDA diagnostic laboratories [NADC, NVSL, MARC] confirmed that this cow was born in Canada. In response to the confirmatory diagnosis, FSIS initiated a Class II recall of meat from cattle slaughtered on December 9 (as a precaution). Additionally, the herd of origin was quarantined, as well as the herd containing a calf from the infected cow.

S
1
i
d
e
1
3

History: U.S.

- June 2005
 - 12 year old Texas beef cow, Nov 2004
 - Confirmed positive with new BSE testing protocol
- March 2006
 - 10 year old Alabama beef cow
 - "Down" on farm; veterinarian posted and submitted obex for testing
- Both animals born before feed ban; neither entered human food chain

Center for Food Security and Public Health
Iowa State University - 2007

In June 2005, the U.S. announced its first positive case of BSE in a 12 year old cow from a herd in Texas. The animal was born before the United States instituted a ruminant-to-ruminant feed ban in August 1997. This animal never entered the human food chain. An "inconclusive" result on the initial BSE screening test from November 2004 was confirmed as positive by The Veterinary Laboratories Agency in Weybridge, England using Western Blot technology in June 2005. This prompted a change in the testing and confirmatory procedure for BSE in the U.S. (see slide 29 for more details) A 10 year old Alabama beef cow was confirmed positive in March 2006 after being down on the home farm and a veterinarian submitted the obex for testing. Both of these U.S. cases were in animals greater than ten years of age; meaning they were born before the ruminant feed ban. It is important to note that neither

animal entered the human food chain.

Details related to Texas case:

http://www.aphis.usda.gov/newsroom/hot_issues/bse/downloads/bse_final_epi_report8-05.pdf

Details related to the Alabama case:

http://www.aphis.usda.gov/newsroom/hot_issues/bse/downloads/EPI_Final5-2-06.pdf

S
1
i
d
e
1
4

Economic Impact

- United Kingdom
 - £3.7 billion total by end of 2001-02
 - In 1996-97
 - £850 million for compensation
 - Prior to 1996
 - £288 million on research, surveillance, compensation
- Very costly, far reaching disease

Center for Food Security and Public Health
Iowa State University - 2007

The United Kingdom has experienced the worst outbreak of BSE, with the peak occurring in 1993. In April of 2000, their government estimated the crisis would cost £ 3.7 billion by the end of the 2001/2002 financial year. Compensation alone in 1996/97 was approximately £ 850 million. Prior to that, the government had spent £ 288 million on research, surveillance, compensation, and other related items. It is a very costly disease that has repercussions far beyond lost meat production.

S
1
i
d
e
1
5

Economic Impact

- United States
- December 2003
- 53 countries banned U.S. imports
- Japan, Mexico, South Korea, Canada
 - 88% of U.S. exports - 2003
- Estimated U.S. losses
 - \$45 to \$66 per head

Center for Food Security and Public Health
Iowa State University - 2007

A May 2005 Kansas State University report estimated the economic impact of the first case of BSE in the U.S. In 2003, US beef exports were valued at \$3.95 billion and accounted for 9.6% of US beef production. In response to the late December 2003 news that a cow in the U.S. had tested positive for BSE, 53 countries banned imports of US cattle and beef products. These bans included such major markets as Japan, Mexico, South Korea, and Canada. These top four markets accounted for 88% of the value of U.S. beef exports during 2003. These import bans have caused US beef exports to drop; quantities for 2004 declined 82% below the 2003 level. While some important markets, including Mexico and Canada, reopened in 2004, the U.S. did not regain access to the Japanese and South Korean beef export markets in 2004, which were the second and third largest markets for US beef in 2003. If the US had regained access to these two key markets and 2004 exports would have been the same as 2003, wholesale revenue per head would have increased between \$45 and \$66 for every cow slaughtered in the U.S. The KSU economists reported minimal impact on domestic markets from the initial U.S. case and, as of July 2005, it remains to be seen how the first case in an indigenous animal will affect foreign and domestic markets.

S
1
i
d
e
1
6

Economic Impact

- First Canadian case
 - Initial 4 month ban
 - Mid-May to mid-September 2003
 - \$2.5 billion
 - Trade losses alone at \$1.5 billion
 - Direct costs
 - Feed, lower prices, reduced sales, disposal of surplus animals
 - Harvest/packaging plants

Center for Food Security and Public Health
Iowa State University - 2007

This economic estimate of the impact of the first occurrence of BSE in Canada was initially estimated to cost the country and its producers upwards of \$2.5 billion dollars, depending on the length of any trade bans. This includes direct costs such as feed, lower prices and reduced sales of cattle, and disposal of surplus animals. Also affected are the harvest and packaging plants due to scale-back/lay-offs, lost revenue and disposing of surplus product. Finally, other sectors such as bovine genetics and the dairy industry were financially hit. Trade losses alone were estimated to account for \$1.5 billion of the total loss. The economic impact of more recent cases of BSE remains to be seen. **NOTE: This economic information has not been updated**

S
l
i
d
e

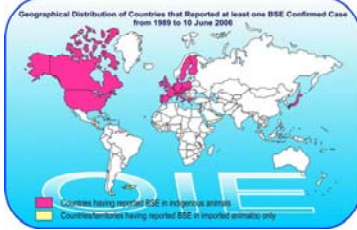
Epidemiology



1
7

S
l
i
d
e

Geographic Distribution



This map depicts the countries that have reported BSE from 1989 to June 2006. The countries shaded pink have had BSE in indigenous animals. They include Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Israel, Italy, Japan, Lichtenstein, Luxembourg, Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, Switzerland, United Kingdom and the United States. Map accessed at the OIE website on July 10, 2007 http://www.oie.int/eng/info/en_esbcarte.htm

1
8

S
l
i
d
e

Geographic Distribution

- 95% of all BSE cases in U.K.
 - Outside U.K. due to importation or contaminated feed
- No cases reported from
 - Australia, New Zealand, Central America, South America
- 2003
 - Canada had first indigenous cases (2)
- 2005
 - Additional Canadian case
 - U.S. reported single case - June

Center for Food Security and Public Health
Iowa State University - 2007

It is important to note that over 95% of the total number BSE cases have developed in the U.K. All cases outside of the UK appear to be a result of importation of live cattle or more significantly, from contaminated feed from the UK. BSE has not been detected in Australia, New Zealand, Central America or South America. In 2003, Canada reported its first indigenous cases (2). In 2005, Canada had an additional case of BSE diagnosed and the US reported its first indigenous case.

1
9

S
l
i
d
e

Transmission



2
0

S
l
i
d
e

Animal Transmission

- Reasons for emergence under debate
 - Feed contaminated with scrapie or unknown BSE
 - Spontaneous
 - Changes in feed processing
- Maternal transmission
 - Possible, low risk
 - Retrospective offspring culling
- Current thought
 - Spread via ingestion of BSE contaminated feed



Center for Food Security and Public Health
Iowa State University - 2007

The exact mechanism responsible for the emergence of BSE in cattle is still under debate. BSE may have occurred by feeding cattle feed that was infected with scrapie products or an unknown TSE. Another theory is that BSE spontaneously emerged in cattle and that this agent was fed back to cattle through the rendering process leading to widespread dissemination and the epidemic. Changes in rendering operations in the early 1980's, particularly the removal of a solvent extraction process that included a steam heat treatment, may or may not have played a role in the appearance of BSE and the subsequent amplification of the agent in the cattle population. After reviewing years of epidemiological data, offspring of clinical BSE cases have an increased risk of developing the disease, but it is still uncertain whether it is true maternal transmission or a genetic susceptibility to acquiring infection from a feed source. As a precaution, retrospective offspring culling of

2
1

infected dams has occurred since 1997. BSE cases detected in other countries appear to be a result of importation of live cattle or more significantly contaminated feed from the UK. The occurrence of transmissible spongiform encephalopathies in Europe in captive bovid, cats and monkeys is believed to have resulted from BSE contaminated feed.

S
1
i
d
e
2
2

Human Transmission

- Humans consuming cattle products infected with BSE can develop vCJD
 - Brain and spinal tissue
- Dose required not known
- Genetic susceptibility
 - All human cases have been homozygous for methionine at codon 129 of PrP^C



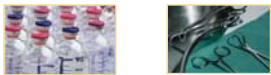
Center for Food Security and Public Health
Iowa State University - 2007

The first confirmed case of variant Creutzfeldt Jakob Disease (vCJD) (human form of BSE) was diagnosed in the UK in March 1996. It is widely accepted that (vCJD) occurs by eating cattle products (primarily brain and spinal tissue) infected with BSE. The dose of infected material required to cause the disease is not known at this time. Genetic susceptibility may play a role in the development of vCJD. To date all cases of human infection have been homozygous for methionine at codon 129 of the prion protein gene (PrP^C).

S
1
i
d
e
2
3

Human Transmission

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



Center for Food Security and Public Health
Iowa State University - 2007

Other possible modes of transmission in humans may be possible. Since abnormal prions are extremely resistant, they persist on surgical instruments despite autoclaving and sterilization procedures. Many instruments used in brain surgery are disposable for this reason. Human and veterinary vaccines prepared from bovine materials may also carry the risk of transmission of animal TSE agents. For this reason, the World Health Organization (WHO) recommends that the pharmaceutical industry should ideally avoid the use of bovine materials and materials from other animal species in which TSEs naturally occur. If absolutely necessary, bovine materials should be obtained from countries which have a surveillance system for BSE in place and which report either zero or only sporadic cases of BSE. These precautions apply to the manufacture of cosmetics as well.

S
1
i
d
e
2
4

Animals and BSE



S
1
i
d
e
2
5

Clinical Signs

- Incubation: 2-8 years
- Initial neurological signs
 - Apprehension, fear, easily startled, depressed
- Final stages
 - Excitable, hyperreflexia, hypermetria, ataxia, muscle fasciculation, tremors

Center for Food Security and Public Health
Iowa State University - 2007

The incubation period for BSE in cattle is 2 to 8 years. The clinical signs are mainly neurological, such as apprehension, fear, being easily startled or depression. During the final stages of disease, infected animal generally shows increased excitability, hyperreflexia, and hypermetria, as well as ataxia, muscle fasciculations, tremors and myoclonus.

S
1
i
d
e
2
6

Clinical Signs

- Terminal state
 - Decreased rumination
 - Loss of body weight and condition, despite good appetite
- There is no treatment for BSE
- Affected herds
 - 2% morbidity
 - 100% mortality



Center for Food Security and Public Health
Iowa State University - 2007

During the end phase of the disease most animals have decreased rumination, loss of body weight and condition despite a good appetite, bradycardia, and an altered heart rhythm. Currently, there is no treatment for BSE. In affected herds of animals, 2% could develop clinical signs. BSE is a fatal disease once symptoms appear with mortality at 100%. Photo depicts a cow in the end stages of BSE struggling to rise. She has lost quite a bit of body condition. Photo source: <http://exn.ca/news/Images/19970428-cow.jpg>

S
1
i
d
e
2
7

Diagnosis

- Slowly progressive, fatal neurologic disease
- Differentials
 - Nervous ketosis, hypomagnesemia, listeriosis, poliоencephalomalacia, rabies, brain tumor, lead poisoning spinal cord trauma
- No antemortem testing available
- Brain, medulla, spinal cord, brain stem

Center for Food Security and Public Health
Iowa State University - 2007

In any animal that develops a slowly progressive neurologic disease, BSE could be the cause, especially if it is fatal. Differentials for BSE include nervous ketosis, hypomagnesemia, listeriosis, poliоencephalomalacia, rabies, intra-cranial tumors, trauma to the spinal cord, and lead poisoning. There is no antemortem testing currently available for BSE. For post-mortem examination, the whole brain, brain stem, or medulla should be extracted as soon as possible after death for histopathology. For specific PrP^{Sc} detection, cervical spinal cord or caudal medulla should be extracted and frozen soon after death. The obex is the portion of the brain that is tested for prions and it is pictured in the photo.

S
1
i
d
e
2
8

Sampling



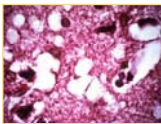
Center for Food Security and Public Health
Iowa State University - 2007

Brain. The red box indicates the region of the obex, which is 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. **Credit:** Dr. S. Sorden, Iowa State University, College of Veterinary Medicine, Department of Veterinary Pathology.

S
1
i
d
e
2
9

Post Mortem Diagnosis

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



Center for Food Security and Public Health
Iowa State University - 2007

The post mortem diagnosis for BSE is microscopic examination of the brain tissue looking for characteristic bilaterally symmetrical spongiform changes in the gray matter and detection of the prion protein using immunohistochemistry. Pictured is a brain demonstrating the "holes" or spongiform changes in the gray matter.

S
1
i
d
e
3
0

Post Mortem Tests for BSE

- All are based on antibodies to detect prion protein in tissue
- Immunohistochemistry (IHC) is considered the gold standard
 - Internationally recognized
 - Expensive, labor intensive
- Rapid diagnostic tests have also been developed
 - Western blotting, ELISA

Center for Food Security and Public Health
Iowa State University - 2007

There are various tests available to detect the presence of the prion agent in nervous tissue. All of these tests rely on antibodies specifically directed against the agent itself. If the prion is present in the tissue tested, these antibodies bind to the agent; if it is not present, they are washed away. Then another test procedure is performed to detect if the antibodies remain, suggesting the prion is present. It is important to note that these tests do not attempt to detect antibodies made by the animal being tested. They use antibodies made through laboratory procedures involving other animals to test tissues from cattle. Immunohistochemistry (IHC) is considered the "gold standard", because it has proven reliable and accurate. It is internationally recognized as the confirmatory test for

BSE. However, it is expensive and requires time and expertise to perform. Various rapid diagnostic tests have been developed that are cheaper, easier to perform and appear to have good diagnostic value, such as the Western blot test and the ELISA.

S
1
i
d
e
3
1

Post Mortem Tests for BSE

- June 24, 2005
 - New BSE confirmatory testing protocol
- IHC & Western Blot confirmatory tests
 - Positive result on either test considered positive for BSE
 - "Inconclusive" BSE rapid screening tests

Center for Food Security and Public Health
Iowa State University - 2007

On June 24, 2005, Agriculture Secretary Mike Johanns announced a new BSE confirmatory testing protocol. Effective that date, if another BSE rapid screening test shows "inconclusive" findings; **both** the IHC and Western blot confirmatory tests will be run by the USDA. If **either** confirmatory test shows a positive result, the sample will be considered positive for BSE. For more information about the IHC and Western Blot tests, visit: http://www.aphis.usda.gov/publications/animal_health/content/printable_version/faq_BSE_confirmtests.pdf

S
1
i
d
e
3
2

Rapid Diagnostic Tests

- *Not* food safety tests
- *Not* valid for assuring absence of prion protein in individual animal
- Antibody-based tests can detect prion protein before spongiform changes occur

Center for Food Security and Public Health
Iowa State University - 2007

It is important to remember that these tests are NOT food safety tests. They do not test the edible product - the meat; they test the brain. And it is uncertain at what stage of disease an animal has to be to test positive. Thus we cannot be certain that the absence of detectable prion means that there is none there. It has been proven that the rapid tests can detect the prion before the spongiform holes develop in the brain. They can also detect the agent before the animal shows signs of the disease. However, it is not known how much prion protein has to be present to be detected.

S
1
i
d
e
3
3

Sampling

- Sampling will be conducted by:
 - State/Federal animal health personnel
 - State/Federal public health personnel
 - Accredited veterinarians
 - Trained state/APHIS contractors

Center for Food Security and Public Health
Iowa State University - 2007

Sampling will be conducted by state/federal animal health or public health personnel, accredited veterinarians, trained state or APHIS contractors. The National Veterinary Services Laboratory will initially be responsible for training collectors in the use of the rapid screening tests, and once trained these individuals will be able to train additional sample collectors.

S
1
i
d
e
3
4

Sampling

- Collection sites:
 - State or Federal slaughter plants
 - On farm
 - Rendering facilities
 - Veterinary diagnostic laboratories
 - Animal feed slaughter facilities
 - Pet food plants
 - Sale barns, livestock auctions
 - Sites utilized by accredited veterinarians

Center for Food Security and Public Health
Iowa State University - 2007

The goal of the enhanced surveillance program is to test as many high-risk cattle as possible by collecting at multiple sites. This would include State or Federal slaughter plants, on farm, rendering facilities, veterinary diagnostic laboratories, animal feed slaughter facilities (pet food plants), sale barns, livestock auctions, and sites utilized by accredited veterinarians.

S
l
i
d
e

BSE in Humans



3
5

S
l
i
d
e

Variant Creutzfeldt Jakob Disease (vCJD)

- Consuming BSE contaminated foods
- 1996, UK: First confirmed case
- Incubation period not known
- Mean age at death
 - 28 years old
- Mean duration of infection
 - 14 months

Center for Food Security and Public Health
Iowa State University - 2007

Currently, it is thought that people who ingest BSE contaminated food products may develop variant Creutzfeldt Jakob Disease (vCJD). The first confirmed case of vCJD occurred in 1996 in the UK. The incubation period for vCJD is unknown because it is a relatively new disease, but it is likely to be many years or decades. Therefore, a person who develops vCJD likely would have consumed an infected product or products many years earlier. In contrast to classic CJD, the variant form (vCJD) in the UK predominantly affects young people with 28 years as the mean age at death. The mean duration of infection is 14.1 months for vCJD.

S
l
i
d
e

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

Center for Food Security and Public Health
Iowa State University - 2007

vCJD has atypical clinical features (as compared to CJD), with prominent psychiatric or sensory symptoms at the time of clinical presentation. Onset of neurological abnormalities is delayed and include ataxia within weeks or months. Dementia and myoclonus occur later in the illness. Affected persons generally become completely immobile and mute at the end stage of the disease.

3
7

S
l
i
d
e

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%)

Center for Food Security and Public Health
Iowa State University - 2007

Classic CJD is a sporadic encephalopathy affecting humans that occurs worldwide at a rate of 1-2 cases per million people. It can occur spontaneously, genetically, or iatrogenically. This disease is not caused by eating BSE contaminated food products. Average age at onset is 65 years which is much older than vCJD. The duration of illness is shorter at 4.5 months. The spontaneous form occurs in about 85% of cases, the genetic form occurs in 5-15% of the cases, and the iatrogenic form (passed unintentionally from a medical procedure) occurs in less than one percent of the cases. An example of an iatrogenic infection has occurred during dura matter grafts where a piece of infected brain tissue is grafted into a healthy persons brain. Another example has occurred when previously healthy people have been injected with gonadotropic hormones that were prepared from the pituitary glands of people infected with CJD.

3
8

S
1
i
d
e
3
9

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



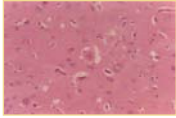
Center for Food Security and Public Health
Iowa State University - 2007

The United Kingdom has established antemortem diagnostic criteria for vCJD and it includes a progressive neuropsychiatric disorder with duration of illness greater than 6 months with no alternative diagnosis or history of iatrogenic exposure. Also, early psychiatric symptoms such as depression, anxiety, apathy, withdrawal and delusions, persistent painful sensory symptoms, ataxia, myoclonus, and dementia. An electroencephalogram (EEG) that rules out sporadic CJD, a positive tonsil biopsy, and spongiform changes in the brain are definitive diagnostic criteria.

S
1
i
d
e
4
0

Diagnosis: vCJD

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



Center for Food Security and Public Health
Iowa State University - 2007

On post mortem exam, examination of the brain should show the following neuropathological features: numerous widespread amyloid plaques surrounded by vacuoles, spongiform changes most often seen in the basal ganglia and thalamus, prion protein accumulation shown by immunocytochemistry, especially in the cerebellum. Image: Large kuru-type plaque surrounded by a zone of spongiform change in a cerebral cortical- biopsy specimen (center). A smaller plaque is also present (right) but spongiform change is sparse. For reference, kuru is a spongiform encephalopathy that affected humans in Papua, New Guinea in the early 1900's. Those people practiced cannibalism as a funeral rite and were afflicted with the same type of brain lesions; hence, kuru- type plaque. Photo courtesy of APHIS-USDA at www.aphis.usda.gov

S
1
i
d
e
4
1

Treatment: vCJD

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

Center for Food Security and Public Health
Iowa State University - 2007

There is no known effective treatment for vCJD though there is experimental treatment taking place with Quinacrine. Since this drug effectively crosses the blood-brain barrier there is hope that it will show some effectiveness. Supportive treatment and symptomatic care are recommended.

S
1
i
d
e
4
2

Public Health Significance

- 1996-2006
 - 200 cases of vCJD worldwide
 - 11 countries
 - 161 cases from UK
- No cases of indigenous vCJD in U.S.
- Unknown incubation period and consumption
 - Possibly more cases of vCJD in future

Center for Food Security and Public Health
Iowa State University - 2007

From 1996 (when the first suspected cases of vCJD occurred) to November 2006, 200 cases of vCJD have been reported worldwide in 11 countries; 164 of which occurred in the UK. There has been no confirmed case of vCJD originating in the United States. Mathematical models have been used to try to predict the magnitude of human infection. These models predict anywhere from hundreds of people being infected to hundreds of thousands of people developing the disease. Given the unknown incubation period and consumption rate that may have occurred, there could be even more vCJD cases in the future. Worldwide statistics from: http://www.cdc.gov/ncidod/dvrd/vcjd/factsheet_nvcjd.htm and U.K. statistics from: <http://www.cjd.ed.ac.uk/figures.htm>

S
l
i
d
e

4
3

Prevention and Control



S
l
i
d
e

4
4

U.S. Government Precautions

- 1989: Import restrictions
 - Live ruminants and ruminant products
 - From countries known to have BSE



Center for Food Security and Public Health
Iowa State University - 2007

The United States government has a number of stringent safeguards in place to prevent the spread of BSE in the US. In 1989, they banned the importation of live ruminants and restricted many ruminant products from countries where BSE was known to exist, including the U.K. These regulations were expanded to include all of Europe in December of 1997.

S
l
i
d
e

4
5

U.S. Government Precautions

- 1990: Targeted surveillance
 - High risk animals
 - Adult animals with neurological signs
 - Non-ambulatory "downer" cows
 - Rabies- negative cattle
 - Cattle dying on farms



Center for Food Security and Public Health
Iowa State University - 2007

The United States has had a targeted surveillance program for BSE in place since May 1990. BSE is a notifiable disease and the Food Safety Inspection Service (FSIS) along with the Animal and Plant Health Inspection Service (APHIS) coordinate testing of high risk animals, including downer animals (animals that are non-ambulatory at slaughter, pictured above), animals that die on the farm, older animals and animals exhibiting signs of neurological distress. Photo courtesy of APHIS-USDA at www.aphis.usda.gov.

S
l
i
d
e

4
6

U.S. Government Precautions

- 1997
 - Import restrictions expanded to include all European countries
 - FDA "animal feed rule"
 - Banned most mammalian proteins as food source for ruminants
- 2002: 19,000 animals tested for BSE
- 2003: 20,000 animals tested for BSE
 - 47 times the number required by OIE

Center for Food Security and Public Health
Iowa State University - 2007

In August 1997, the FDA instituted regulations to prohibit the use of most mammalian protein, with a few exceptions, in ruminant animal feeds. The "animal feed rule" exempts the following products: blood and blood byproducts, milk products, pure porcine and pure equine products, plate waste, tallow, gelatin and non-mammalian protein (poultry, marine, vegetable). During fiscal years of 2002 and 2003, the USDA tested 19,990 animals and 20,000 respectively. Both of these figures are significantly higher than the standards set by the Office International des Epizooties (OIE), the standard setting organization for animal health for 166 member nations. Under the international standard at that time, a BSE-free country (the status of the US prior to Dec. 2003) would only be required to test 433 head of cattle per year.

S
l
i
d
e

4
7

U.S. Response to Its First Case

- Dec 30, 2003: Additional safeguards
 - All downer cattle banned from human food
 - Suspect cattle carcass held until BSE test results received
 - Specified Risk Material (SRM) prohibited from human food chain
 - Cattle over 30 months of age
 - Skull, brain, trigeminal ganglia, eyes, vertebral column, spinal cord, dorsal root ganglia
 - All cattle: distal ileum and tonsils

Center for Food Security and Public Health
Iowa State University - 2007

Even though effective safeguard measures were already in place in the US, the Secretary of Agriculture, Ann Veneman, announced on December 30, 2003, additional safeguards being implemented due to an abundance of caution, to further strengthen protections against BSE in the U.S.

All downer cattle presented for slaughter will be banned from the human food chain. Additionally any suspect cattle will be held until BSE tests are confirmed.

Specified Risk Material (SRM) will also be prohibited from the human food chain. This material includes the skull, brain, trigeminal ganglia, eyes, vertebral column, spinal cord and dorsal root ganglia

of cattle over 30 months of age. Additionally, the distal ileum and tonsils (which are already prohibited) from all cattle will be prohibited.

S
1
i
d
e
4
8

U.S. Response to Its First Case

- Additional process control for AMR (advanced meat recovery) system
 - Prohibition of spinal cord tissue, dorsal root ganglia, and skull
 - Routine testing by FSIS
- Prohibition of air-injection stunning of cattle at slaughter
- Implementation of national animal identification plan

Center for Food Security and Public Health
Iowa State University - 2007

Additional process controls have been determined for AMR (advanced meat recovery) systems. Prior regulations prohibited spinal cord tissue in product going into the human food chain. This was routinely verified by FSIS officials through testing of product. Regulations have now been expanded to prohibit dorsal root ganglia, skull, as well as any spinal cord tissue in processing. The use of air-injection stunning of cattle at slaughter has also been prohibited immediately to reduce the potential of brain tissue being dislocated into the tissue of carcasses. Additionally, a national animal identification plan (which was previously being developed) will be implemented and, as of July 2005, this national animal ID plan is still in the implementation stage.

S
1
i
d
e
4
9

U.S. Government Precautions

- Enhanced Surveillance for BSE
 - June 2004 to March 2006
- High risk cattle
 - Non-ambulatory
 - CNS problems
 - BSE signs- wasting, injury
 - Dead
- 667,767 tested (20K healthy cattle)
 - 2 positives (0.0003% test positive)

Center for Food Security and Public Health
Iowa State University - 2007

In June 2004, the USDA designed and implemented an Enhanced BSE Surveillance Program to determine the level of disease present in the US cattle population. This surveillance was aimed at testing high risk cattle (those showing CNS signs, dead, non-ambulatory) with an estimated population of over 445,000 adults per year. From June 2004 to March 2006, 647,045 samples were collected from 5,776 unique locations including slaughter plants, renderers, farms, public health labs, vet diagnostic labs, and salvage slaughter plants. Of these samples, 2 were confirmed positive (0.0003% test positive). In addition to the high risk, targeted population, an additional 20,722 animals were tested for a total of 667,767. Information obtained March 25, 2007 from http://www.aphis.usda.gov/newsroom/hot_issues/bse/downloads/SummaryEnhancedBSE-Surv4-26-06.pdf

S
1
i
d
e
5
0

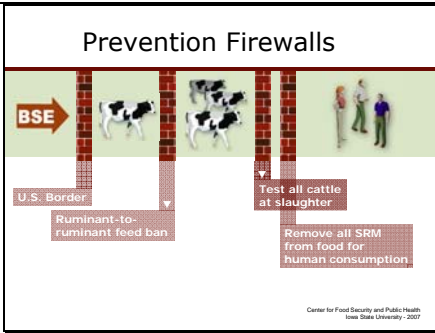
U.S. Government Precautions

- Ongoing Surveillance for BSE
 - Sept 2006 to current
- High risk cattle
 - CNS signs
 - >30 months in poor health, non-ambulatory, dead, or with BSE signs- wasting, injury, dead
- 33,141 tested (goal 40,000/yr)
 - 0 positives as of June 2007

Center for Food Security and Public Health
Iowa State University - 2007

The USDA implemented the Ongoing BSE Surveillance Program in 2006 and it focuses on being able to detect BSE at 1 infected animal per 1,000,000 adult cattle with a high degree of confidence. This program will sample more animals than what the OIE recommends and collects samples from cattle populations where BSE is most likely to be detected (those with CNS signs, greater than 30 months of age with BSE signs, injured, non-ambulatory, dead) with the goal of 40,000 per year. From Sept 2006 through June 2007, 33,141 samples were collected and there were no positives (information source http://www.aphis.usda.gov/newsroom/hot_issues/bse/surveillance/ongoing_surv_results.shtml). Ongoing BSE Surveillance Information obtained March 25, 2007 from http://www.aphis.usda.gov/newsroom/hot_issues/bse/downloads/BSE_ongoing_surv_plan_final_71406%20.pdf

S
1
i
d
e
5
1



Recognition of BSE transmission routes enables the formation of “firewalls” to help prevent and control the disease. If any single firewall is considered completely effective, no other precautions would be necessary, making comprehensive knowledge of transmission routes essential to preventing BSE in the United States. By applying these preventative measures to our current system we help prevent and control the disease.

The first firewall is prevention of the disease entering the country. We have previously discussed the various methods the U.S. has in place.

The second firewall is prohibition of potentially infectious materials (ruminant feed products) from entering the cattle feed supply. This prevents amplification within the national herd, and was instituted in the U.S. in 1997.

The third firewall is to remove specified risk materials (SRM) from all carcasses, so that no infectious material can enter the food supply. This was instituted in 2004.


Testing all cattle at slaughter could be considered a potential firewall for preventing BSE. However, with three very effective firewalls in place (protecting the U.S. border, the ruminant-to-ruminant feed ban, and removal of all SRM) and given the absence or very low incidence of BSE in the U.S., testing all animals has no preventative value because U.S. beef is already safe to eat.

Graphic designed by Clint May, ISU.

S
1
i
d
e
5
2

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



Center for Food Security and Public Health
Iowa State University - 2007

Due to the serious economic and human repercussions of this disease, authorities should be notified immediately of any suspicious cases of BSE. As the meat from the animal should never enter the human food chain, the brain and medulla should be submitted for necropsy and the carcass properly disposed of/ incinerated. Use extreme caution while extracting the brain so as not to expose yourself. While waiting for a confirmatory diagnosis, all suspect animals should be quarantined. Should BSE be confirmed diagnostically, depopulation and trace backs will occur. Proper disposal of all suspect animals is essential so their products are not allowed to enter the human food chain.

S
1
i
d
e
5
3

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.html
- Quarantine

Center for Food Security and Public Health
Iowa State University - 2007

If you suspect a case of BSE, contact your state and/or federal veterinarian immediately and establish a quarantine of the premise.

S
l
i
d
e

5
4

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 at high temperature and pressure
- Resistant in tissues, dried organic material, high titer



Center for Food Security and Public Health
Iowa State University - 2007

To physically inactivate the prion, the best option is porous load autoclaving at 134-138°C for 18 minutes (pictured above). It is important to note that this temperature range may not completely inactivate the prion. Some disinfectants listed include sodium hypochlorite with 2% available chlorine, or 2 N sodium hydroxide applied for more than 1 hour at 20°C on surfaces and 8 hours for equipment. Rendering at 133°C at 3 bar pressure for a minimum of 20 minutes is used in Great Britain. The prion is very resistant if it is in tissues, dried organic material or at a very high titer. Equipment used for brain and spinal cord surgery in the U.K. is disposed of as they felt the risk was too high to try and disinfect and reuse, thus adding cost to these procedures. Information obtained from the OIE website at http://www.oie.int/eng/maladies/fiches/a_B115.htm

S
l
i
d
e

5
5

Vaccination/Prevention

- No effective treatment or vaccine
- Surveillance program
- Blood/plasma donation restrictions
 - 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/cjdvcd.pdf

Center for Food Security and Public Health
Iowa State University - 2007

Currently no effective treatment is available, however experimental drugs are under investigation. In response to the threat of BSE, the CDC has activated a surveillance program in the U.S. Additionally, the Red Cross has restricted blood and plasma donations from persons who have traveled or lived for 3 or more cumulative months in the U.K. between the years of 1980 to 1996. Military personnel who resided on bases in Germany, U.K. Belgium and the Netherlands for 6 months or more between 1980 and 1990 should be deferred indefinitely from donations. Other military personnel living on bases in Greece, Turkey, Spain, Portugal, and Italy for 6 months or more between 1980 and 1996 should also be deferred. For more information, please access the FDA website www.fda.gov/cber/gdlns/cjdvcd.pdf

S
l
i
d
e

5
6

Additional Resources



S
l
i
d
e

5
7

Internet Resources

- U.S. Department of Agriculture
 - www.aphis.usda.gov
- World Organization for Animal Health (OIE) website
 - www.oie.int
- Canadian Food Inspection Agency
 - www.inspection.gc.ca/english/animas/heasan/disemala/disemalae

Center for Food Security and Public Health
Iowa State University - 2007

S
l
i
d
e
5
8

Acknowledgments

Development of this presentation was funded by a grant from the Centers for Disease Control and Prevention to the Center for Food Security and Public Health at Iowa State University.

Center for Food Security and Public Health
Iowa State University - 2007

S
l
i
d
e
5
9

Acknowledgments

Author: Danelle Bickett-Weddle, DVM, MPH

Co-authors: Jamie Snow, DVM, MPH
Glenda Dvorak, DVM, MS, MPH
Jared Taylor, DVM
Bryan Buss, DVM
Anna Rovid-Spickler, DVM, PhD

Reviewers: James Roth, DVM, PhD
Radford Davis, DVM, MPH
Bindy Comito Sornsin, BA

Last updated: July 10, 2007
Center for Food Security and Public Health
Iowa State University - 2007