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Bovine Spongiform Encephalopathy
Mad Cow Disease

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Overview

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



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.

[Photo: Holstein cow. Source: Peggy Greb-USDA-ARS]

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THE ORGANISM

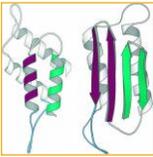
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Prion

- 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

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 I i d e 5	<p style="text-align: center;">Normal protein</p> <ul style="list-style-type: none"> • Secondary structure dominated by alpha helices • Easily soluble • Easily digested by proteases • Encoded by PRNP gene (in humans) <ul style="list-style-type: none"> - Located on human chromosome 20 	<p>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.</p>
S I i d e 6	<p style="text-align: center;">Abnormal Protein</p> <ul style="list-style-type: none"> • PrP^{Sc} (Sc for scrapie) <ul style="list-style-type: none"> - Same amino acid sequence and primary structure as normal protein - Secondary structure dominated by beta conformation • When PrP^{Sc} contacts PrP^C <ul style="list-style-type: none"> - Converts it to the abnormal form 	<p>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. However, 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 the abnormal form. This diagram depicts the normal prion on left and the abnormal prion on right.</p> <p>[Photo: This photo shows a 3-dimensional image of a normal prion (left) and abnormal prion (right). The normal prion protein (left) has many alpha-helix regions that are fairly soluble while the abnormal prion protein (right) has many beta-pleated sheet regions and make it insoluble. Source: A</p>
S I i d e 7	<p style="text-align: center;">Abnormal Protein</p> <ul style="list-style-type: none"> • Insoluble in all but strongest solvents • Highly resistant to digestion by proteases <ul style="list-style-type: none"> - Survives in tissues post-mortem • Extremely resistant <ul style="list-style-type: none"> - Heat, normal sterilization processes, sunlight • No detectable immune response 	<p>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 over a wide pH range. The abnormal protein does not evoke a detectable immune or inflammatory response in its host, so the body does not react to it as an invader.</p>
S I i d e 8	<p style="text-align: center;">Abnormal Protein</p> <ul style="list-style-type: none"> • Atypical BSE prions <ul style="list-style-type: none"> - H-type: high molecular mass fragments - L-type (bovine amyloidotic spongiform encephalopathy [BASE]): lower molecular mass fragments - May represent additional strains or spontaneously occurring prions 	<p>In addition to the 'classical' BSE prion, at least two atypical BSE prions can be found in cattle. One has higher molecular mass fragments than classical BSE and is called 'H-type'; the other has a lower molecular mass and is called 'L-type' or bovine amyloidotic spongiform encephalopathy (BASE). Atypical BSE prions may represent additional strains of BSE or spontaneously occurring prions.</p>

S l i d e 9	<p>IMPORTANCE</p>
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S l i d e 1 0	<p>History</p> <ul style="list-style-type: none"> • 1986 <ul style="list-style-type: none"> - First confirmed case in United Kingdom • 1988 <ul style="list-style-type: none"> - U.K. bans meat and bone meal from ruminants in cattle feed • 1989 <ul style="list-style-type: none"> - USDA bans importation of ruminants from countries with BSE 	<p>The first confirmed case of BSE occurred in 1986 in the United Kingdom. Following that discovery, in 1988 the U.K. 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 U.K. and continue today.</p>
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S l i d e 1 1	<p>History</p> <ul style="list-style-type: none"> • 1993 <ul style="list-style-type: none"> - Peak of BSE in U.K • 1997 <ul style="list-style-type: none"> - U.S. and Canada ban feeding ruminant products to ruminants - U.S. importation ban extended to all of Europe regardless of BSE status • 2001 <ul style="list-style-type: none"> - E.U. orders mandatory tests on cattle > 30 months old 	<p>The peak incidence of BSE in the U.K. 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; by 2009, only 9 cases were reported). 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.</p>
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(Information on U.K. case numbers obtained: http://www.oie.int/eng/info/en_esbru.htm)

S l i d e 1 2	<p>History: Canada</p> <ul style="list-style-type: none"> • 1993: 1 case (imported from U.K.) • 2003: 2 cases (one living in U.S.) • 2004, 2005: 1 case each year • 2006: 5 cases • 2007: 3 cases • 2008: 4 cases • 2009: 1 case • 2010: 1 case (as of 6/2010) 	<p>Canada's first case of BSE occurred in 1993 in a single cow imported from the U.K. In 2003, 2 cases of BSE were diagnosed in indigenous cattle - the first occurring on May 20, 2003 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 <u>time from slaughter to diagnosis</u> was due to other priorities, as BSE was not a concern <u>at the time</u>. Tracebacks were done on 40 herds and 2,700 cattle were slaughtered, all of which were over 24 months of age; all were found to be BSE negative.</p>
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In December 2003, a 6 ½ year old Holstein cow tested positive in Washington State in the U.S. 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 were negative. Canada continues to

diagnose BSE as indicated on the slide.

(Status of Canadian cases can be found at:

http://www.oie.int/eng/info/en_esbmonde.htm)

[Photo: cattle grazing. Source: Scott Bauer-USDA-ARS]

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History: U.S.

- December 2003
 - Dairy cow from Washington state
 - Confirmed by DNA tests
 - 6½ years old, imported from Canada
 - Complications following calving and sent to slaughter
- Presumptive positive by NVSL
- Definitively positive by U.K. lab

On December 23, 2003, the U.S. announced the discovery of its first case of BSE. The case involved a 6-1/2 year old dairy cow sent to slaughter on December 9, due to complications following calving (“downer”). The cow was identified prior to slaughter as a BSE suspect for testing. 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 U.K. 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 was the herd containing a calf from the infected cow.

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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

In June 2005, the U.S. announced its first positive indigenous 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, prompting a veterinarian to submit the obex for testing. Both of these U.S. cases involved 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

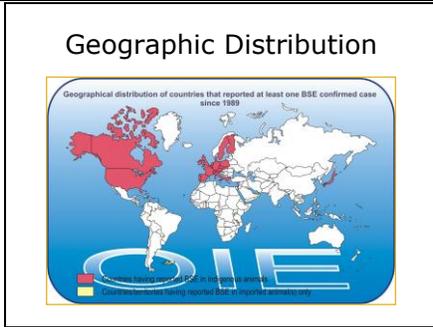
Details related to the Alabama case:

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

<p>S I d e 1 5</p>	<p style="text-align: center;">Economic Impact</p> <ul style="list-style-type: none"> • United Kingdom <ul style="list-style-type: none"> - £3.7 billion total by end of 2001-02 - In 1996-97 <ul style="list-style-type: none"> • £850 million for compensation - Prior to 1996 <ul style="list-style-type: none"> • £288 million on research, surveillance, compensation • Very costly, far reaching disease 	<p>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. BSE is a very costly disease that has repercussions far beyond the lost meat production.</p>
<p>S I d e 1 6</p>	<p style="text-align: center;">Economic Impact</p> <ul style="list-style-type: none"> • United States - December 2003 <ul style="list-style-type: none"> - First U.S. case of BSE - 53 countries banned U.S. imports - Japan, Mexico, South Korea, Canada (88% of U.S. exports in 2003) • Estimated U.S. losses <ul style="list-style-type: none"> - \$45 to \$66 per head 	<p>A May 2005 Kansas State University report estimated the economic impact of the first case of BSE in the U.S. In 2003, U.S. beef exports were valued at \$3.95 billion and accounted for 9.6% of U.S. 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 U.S. 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. Import bans caused U.S. 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 until later. Because of this market loss, whole sale revenue for cattle dropped \$45-\$66 per head in the U.S. Kansas State University economists reported minimal impact on domestic markets from the initial U.S. case.</p>
<p>S I d e 1 7</p>	<p style="text-align: center;">Economic Impact</p> <ul style="list-style-type: none"> • First Canadian case <ul style="list-style-type: none"> - Initial 4 month ban - Mid-May to mid-September 2003 - \$2.5 billion <ul style="list-style-type: none"> • Trade losses alone at \$1.5 billion - Direct costs <ul style="list-style-type: none"> • Feed, lower prices, reduced sales, disposal of surplus animals • Harvest/packaging plants 	<p>The economic impact of the first BSE case in Canada was 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, 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 disposal 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.</p>
<p>S I d e 1 8</p>	<p style="text-align: center;">EPIDEMIOLOGY</p>	

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This map shows the countries that reported at least one BSE confirmed case since 1989. They include the U.S., Canada, most of Europe, and Japan.

[Photo: Map showing the geographical distribution of countries that reported at least one BSE confirmed case since 1989. Source World Organization for Animal Health (OIE) <http://www.oie.int/animal-health-in-the-world/bse-specific-data/map/>. Accessed 10-18-2013]

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- Geographic Distribution
- 95% of all BSE cases in U.K.
 - No cases reported from
 - Australia, New Zealand, Central America, South America
 - 2003
 - First indigenous case, Canada
 - 2005
 - Additional Canadian case
 - First indigenous case, U.S.

It is important to note that over 95% of the total number of BSE cases have developed in the U.K. BSE has not been detected in Australia, New Zealand, or Central or South America. In 2003, Canada reported its first indigenous case. In 2005, Canada had an additional case of BSE and the U.S. reported its first indigenous case.

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TRANSMISSION

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- Animal Transmission
- Origin unclear
 - Feed contaminated with scrapie or unknown BSE
 - Spontaneous mutation
 - Changes in feed processing
 - Maternal transmission
 - Possible, low risk
 - Retrospective offspring culling
 - Likely spread ingestion of BSE contaminated feed
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The exact mechanism responsible for the emergence of BSE in cattle is still under debate. Cattle feed may have been contaminated with scrapie products or an unknown TSE. Alternatively, BSE may have spontaneously emerged in cattle with subsequent feed back to other cattle (after rendering). Changes in rendering operations in the early 1980s, 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. 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 infected dams has occurred since 1997. The occurrence of transmissible spongiform encephalopathies in Europe in captive bovids, cats, and monkeys is believed to have resulted from BSE contaminated feed.

[Photo: cattle eating. Source: Scott Bauer-USDA-ARS]

S I d e 2 3	<p style="text-align: center;">Human Transmission</p> <ul style="list-style-type: none"> • Humans consuming cattle products infected with BSE can develop vCJD <ul style="list-style-type: none"> - Brain and spinal tissue • Dose required unknown • Genetic susceptibility <ul style="list-style-type: none"> - All human cases have been homozygous for methionine at codon 129 of PrP^C 	<p>The first confirmed case of variant Creutzfeldt Jakob Disease (vCJD) (human form of BSE) was diagnosed in the U.K. in March of 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). It is not known whether people with resistant genotypes (valine/valine or methionine/valine) are completely resistant to the development of disease, or simply have a longer incubation period.</p>
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S I d e 2 4	<p style="text-align: center;">Human Transmission</p> <ul style="list-style-type: none"> • Possible modes <ul style="list-style-type: none"> - Transmission from surgical instruments used on tonsils, appendix, or brain tissue - Growth hormone injections - Vaccines <div style="display: flex; justify-content: space-around; align-items: center;">   </div>	<p>Other 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.</p>
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S I d e 2 5	<p>ANIMALS AND BSE</p>	
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S I d e 2 6	<p style="text-align: center;">Clinical Signs</p> <ul style="list-style-type: none"> • Incubation: 2 to 8 years • Initial neurological signs <ul style="list-style-type: none"> - Often subtle - Apprehension, fear, easily startled, depressed • Final stages <ul style="list-style-type: none"> - Excitable, hyperreflexia, hypermetria, ataxia, muscle fasciculation, tremors 	<p>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 animals generally show increased excitability, hyperreflexia, and hypermetria, as well as ataxia, muscle fasciculations, tremors, and myoclonus.</p>
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Clinical Signs

- Terminal state
 - Decreased rumination
 - Loss of body weight and condition despite good appetite
- There is no treatment for BSE
- Affected herds
 - 2 to 3% morbidity
 - 100% mortality



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 to 3% could develop clinical signs. BSE is a fatal disease once symptoms appear with mortality at 100%. The photo depicts a cow struggling to rise in the end stages of BSE. She has lost quite a bit of body condition.

[Photo: Cow with BSE. Source: Dr. Art Davis/USDA APHIS via wikimedia-commons.org]

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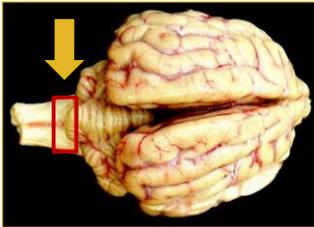
Diagnosis

- 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

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, the 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. (It is pictured in the photo on the next slide.)

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Sampling

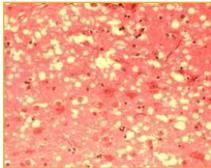


[Photo: Brain. The red box indicates the region of the obex, which is the portion of the brain that must be obtained for the diagnosis of BSE and other spongiform encephalopathies such as scrapie and chronic wasting disease. Source: Dr. S. Sorden, Iowa State University, College of Veterinary Medicine, Department of Veterinary Pathology/CFSPH]

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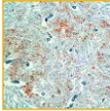
Post Mortem Diagnosis

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



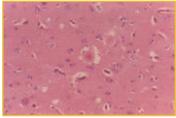
The post mortem diagnosis for BSE is microscopic examination of the brain tissue looking for characteristic bilaterally symmetrical spongiform changes in the gray matter, and detection of the prion protein using immunohistochemistry. Some animals in early stages of infection have no spongiform changes. Amyloid plaques are not typical of classical BSE, but are associated with atypical L-form BSE prions.

[Photo: This micrograph of brain tissue reveals the cytoarchitectural histopathologic changes found in BSE. The presence of vacuoles, i.e. microscopic “holes” in the gray matter, gives the brain of BSE-affected cows a sponge-like appearance when tissue sections are examined in the lab. Source: USDA APHIS]

<p>S I d e 3 1</p>	<p style="text-align: center;">Post Mortem Tests for BSE</p> <ul style="list-style-type: none"> • All are based on antibodies to detect prion protein in tissue • Immunohistochemistry (IHC) is considered the gold standard <ul style="list-style-type: none"> - Internationally recognized - Expensive, labor intensive • Rapid diagnostic tests <ul style="list-style-type: none"> - Western blotting, ELISA 	<p>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. It is important to note that these tests do not attempt to detect antibodies made by the animal being tested (natural antibodies are not produced). 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.</p>
	<p>[Photo: Immunohistochemistry of the brain of a BSE-affected cow using PrP-specific monoclonal antibody. Source: AJ Cann/flickr.creative-commons]</p>	
<p>S I d e 3 2</p>	<p style="text-align: center;">Post Mortem Tests for BSE</p> <ul style="list-style-type: none"> • June 24, 2005 <ul style="list-style-type: none"> - New BSE confirmatory testing protocol • IHC & Western Blot <ul style="list-style-type: none"> - Confirmatory tests - Performed with “inconclusive” BSE rapid screening test results - Positive result on either test considered positive for BSE 	<p>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.</p> <p>(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)</p>
<p>S I d e 3 3</p>	<p style="text-align: center;">Rapid Diagnostic Tests</p> <ul style="list-style-type: none"> • <i>NOT</i> food safety tests • <i>NOT</i> valid for assuring absence of prion protein in individual animal • Antibody-based tests can detect prion protein before spongiform changes occur 	<p>Rapid tests allow large numbers of samples to be screened and are often used in surveillance and slaughter testing. Positive tests are confirmed with more specific assays such as immunohistochemistry or immunoblotting, or by finding characteristic prion fibrils called scrapie-associated fibrils (SAF) with electron microscopy in brain extracts. It is important to remember that these rapid tests are NOT food safety tests. They do not test the edible product - the meat; they test the brain. 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.</p>
<p>S I d e 3 4</p>	<p style="text-align: center;">Sampling</p> <ul style="list-style-type: none"> • 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 <p style="font-size: small; text-align: center;">Center for Food Security and Public Health, Iowa State University, 2011</p>	<p>Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities (state and/or federal veterinarian) should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease. Sampling for BSE surveillance will be conducted by state/federal animal health or public health personnel, accredited veterinarians, or 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.</p>

S I I d e 3 5	<p style="text-align: center;">Sampling</p> <ul style="list-style-type: none"> • Collection sites <ul style="list-style-type: none"> - State or Federal slaughter plants - On farm - Rendering facilities - Veterinary diagnostic laboratories - Animal feed slaughter facilities <ul style="list-style-type: none"> • Pet food plants - Sale barns, livestock auctions - Sites utilized by accredited veterinarians 	<p>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, farms, rendering facilities, veterinary diagnostic laboratories, animal feed slaughter facilities (pet food plants), sale barns, livestock auctions, and sites utilized by accredited veterinarians.</p>
S I I d e 3 6	<p style="text-align: center;">BSE IN HUMANS</p>	
S I I d e 3 7	<p style="text-align: center;">Variant Creutzfeldt Jakob Disease (vCJD)</p> <ul style="list-style-type: none"> • Consuming BSE contaminated foods • 1996, U.K.: First confirmed case • Incubation period not known • Mean age at onset <ul style="list-style-type: none"> - 26 years old • Mean duration of infection <ul style="list-style-type: none"> - 14.1 months 	<p>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 U.K. 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 U.K. predominantly affects young people, with 26 years as the mean age at the onset of symptoms (range 12-74). The mean duration of infection once clinical signs begin is 14.1 months (6 months to 2 years) for vCJD.</p>
S I I d e 3 8	<p style="text-align: center;">Clinical Signs: vCJD</p> <ul style="list-style-type: none"> • Initial symptoms <ul style="list-style-type: none"> - Depression, anxiety, insomnia, social withdrawal, persistent painful sensory symptoms - Schizophrenia-like psychosis - Neurological signs • Progression <ul style="list-style-type: none"> - Become completely immobile and mute 	<p>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.</p>
S I I d e 3 9	<p style="text-align: center;">Classic Creutzfeldt Jakob Disease (CJD)</p> <ul style="list-style-type: none"> • Worldwide • 1 to 2 cases/million people • Not caused by eating BSE contaminated food products • Average age of onset 65 years • Three forms <ul style="list-style-type: none"> - Spontaneous (85%) most common 	<p>Classic CJD is a sporadic encephalopathy affecting humans that occurs worldwide at a rate of 1 to 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 for vCJD. The duration of illness is shorter, being only 4.5 months. The spontaneous form occurs in about 85% of cases, the genetic form occurs in 5 to 15% of the cases, and the iatrogenic form (passed unintentionally from a medical procedure) occurs in less than one percent of the cases. Examples of iatrogenic infection could include receipt of a brain tissue graft from an infected donor or injection of hormones that were prepared from the pituitary glands of people infected with CJD into a healthy patient.</p>

S I d e 4 0	<p style="text-align: center;">Diagnosis: vCJD</p> <ul style="list-style-type: none"> • U.K. criteria for antemortem diagnosis <ul style="list-style-type: none"> - Neuropsychiatric disorder with duration longer than 6 months - Specific clinical signs - Cortical atrophy on MRI - Abnormal EEG - Tonsillar biopsy with detection of prion protein 	<p>The United Kingdom has established antemortem diagnostic criteria for vCJD; 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, as well as persistent painful sensory symptoms, ataxia, myoclonus, and dementia are all highly suggestive. An electroencephalogram (EEG) that rules out sporadic CJD (although EEGs may be normal during early stages of disease), a positive tonsil biopsy, and cortical atrophy on magnetic resonance imaging (MRI) of the brain are definitive diagnostic criteria.</p>
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S I d e 4 1	<p style="text-align: center;">Diagnosis: vCJD</p> <ul style="list-style-type: none"> • Post mortem definitive diagnosis <ul style="list-style-type: none"> - Amyloid plaques surrounded by vacuoles - Prion protein accumulation in cerebellum - Spongiform appearance in gray matter 	<p>On post mortem exam, examination of the brain may show the following features: spongiform changes most often seen in the basal ganglia and thalamus and prion protein accumulation shown by immunocytochemistry, especially in the cerebellum. In addition, widespread amyloid plaques surrounded by vacuoles may be seen in 5-10% of cases with sporadic/genetic CJD).</p> <p>[Photo: This image shows a large kuru-type plaque surrounded by a zone of spongiform change in a cerebral cortical- biopsy specimen. (Kuru is a spongiform encephalopathy that affected humans in Papua, New Guinea in the early 1900s. The people there practiced cannibalism as a funeral rite and were afflicted with the same type of brain lesions; hence, kuru-type plaque.) Source: APHIS-USDA at www.aphis.usda.gov]</p>
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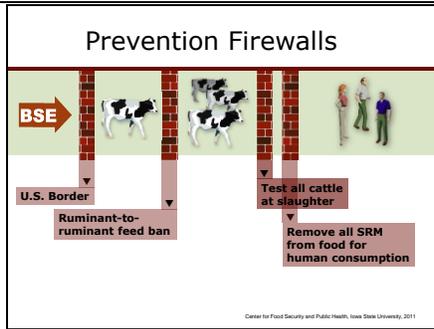
S I d e 4 2	<p style="text-align: center;">Treatment: vCJD</p> <ul style="list-style-type: none"> • No effective treatment available <ul style="list-style-type: none"> - Experimental drugs under investigation • Symptomatic treatment • Supportive care 	<p>There is no known effective treatment for vCJD, though there is experimental treatment taking place. Supportive treatment and symptomatic care are recommended.</p>
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S I d e 4 3	<p style="text-align: center;">Public Health Significance</p> <ul style="list-style-type: none"> • 1996-2009 <ul style="list-style-type: none"> - 217 cases of vCJD worldwide - 11 countries - 170 cases from U.K. • No cases of indigenous vCJD in U.S. • Unknown incubation period and consumption rate 	<p>From 1996 (when the first suspected cases of vCJD occurred) to 2009, 217 cases of vCJD have been reported worldwide in 11 countries. As of 2009, 170 cases have occurred in the U.K. 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.</p> <p>[Photo: Map of the United Kingdom. Source: wikimedia.org]</p> <p>(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)</p>
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<p>S l i d e 4 4</p>	<p style="text-align: center;">PREVENTION AND CONTROL</p>	
<p>S l i d e 4 5</p>	<p style="text-align: center;">U.S. Government Precautions</p> <ul style="list-style-type: none"> • 1989: Import restrictions from countries with known BSE <ul style="list-style-type: none"> - Banned importation of live ruminants - Restricted importation of many ruminant products 	<p>The United States government has a number of stringent safeguards in place to prevent the spread of BSE in the U.S. 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.</p> <p>[Photo: Cattle eating. Source: USDA]</p>
<p>S l i d e 4 6</p>	<p style="text-align: center;">U.S. Government Precautions</p> <ul style="list-style-type: none"> • 1990: Targeted surveillance for "high-risk" animals <ul style="list-style-type: none"> - Adult animals with neurological signs - Non-ambulatory "downer" cows - Rabies-negative cattle - Cattle dying on farms 	<p>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.</p> <p>(Photo courtesy of APHIS-USDA at www.aphis.usda.gov)</p>
<p>S l i d e 4 7</p>	<p style="text-align: center;">U.S. Government Precautions</p> <ul style="list-style-type: none"> • 1997: Import restrictions expanded to include all European countries • 1997: FDA "animal feed rule" <ul style="list-style-type: none"> - Banned most mammalian proteins as food source for ruminants • 2002: 19,990 animals tested for BSE • 2003: 20,000 animals tested for BSE <ul style="list-style-type: none"> - 47 times the number required by OIE 	<p>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 U.S. prior to Dec. 2003) would only be required to test 433 head of cattle per year.</p>

<p>S I d e 4 8</p>	<p>U.S. Response to First Case</p> <ul style="list-style-type: none"> • Dec 30, 2003: Additional safeguards <ul style="list-style-type: none"> - 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 <ul style="list-style-type: none"> • Cattle >30 months of age: neurological tissues • All cattle: distal ileum and tonsils 	<p>Even though effective safeguard measures were already in place in the U.S., Secretary of Agriculture Ann Veneman announced on December 30, 2003 additional safeguards being implemented to further strengthen protections against BSE in the U.S. They include:</p> <ul style="list-style-type: none"> • 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) would 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. The distal ileum and tonsils (which were already prohibited) from all cattle would be prohibited.
<p>S I d e 4 9</p>	<p>U.S. Response to First Case</p> <ul style="list-style-type: none"> • Additional process control for AMR (advanced meat recovery) system <ul style="list-style-type: none"> - Prohibition of spinal cord tissue, dorsal root ganglia, and skull - Routine testing by FSIS • Prohibition of air-injection stunning of cattle at slaughter 	<p>Additional process controls have been determined for AMR (advanced meat recovery) systems. Prior regulations prohibited spinal cord tissue in products going into the human food chain. This was routinely verified by FSIS officials through testing of products. Regulations have now been expanded to prohibit dorsal root ganglia and skull, as well as any spinal cord tissue in processing. The use of air-injection stunning of cattle at slaughter has also been prohibited to reduce the potential of brain tissue being dislocated into the tissue of carcasses.</p>
<p>S I d e 5 0</p>	<p>U.S. Government Precautions</p> <ul style="list-style-type: none"> • Enhanced Surveillance for BSE <ul style="list-style-type: none"> - June 2004 to March 2006 • High risk cattle <ul style="list-style-type: none"> - Non-ambulatory - CNS problems - BSE signs: wasting, injury - Dead • 667,767 tested (20K healthy cattle) <ul style="list-style-type: none"> - 2 positives (0.0003% test positive) 	<p>In June 2004, the USDA designed and implemented an Enhanced BSE Surveillance Program to determine the level of disease present in the U.S. cattle population. This surveillance was aimed at testing high risk cattle (those showing CNS signs, non-ambulatory, dead) 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.</p>
<p>(Information obtained March 25, 2007 from http://www.aphis.usda.gov/newsroom/hot_issues/bse/downloads/SummaryEnhancedBSE-Surv4-26-06.pdf)</p>		
<p>S I d e 5 1</p>	<p>U.S. Government Precautions</p> <ul style="list-style-type: none"> • Ongoing Surveillance for BSE <ul style="list-style-type: none"> - Sept 2006 to current • High risk cattle <ul style="list-style-type: none"> - CNS signs - >30 months in poor health, non-ambulatory, dead, or with BSE signs- wasting, injury, dead • 33,141 tested (goal 40,000/yr) <ul style="list-style-type: none"> - 0 positives as of June 2007 	<p>The USDA implemented the Ongoing BSE Surveillance Program in 2006 which 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 collect 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; no positives were detected. (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)</p>

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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)

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Recommended Actions

- IMMEDIATELY notify authorities
 - Federal
 - Area Veterinarian in Charge (AVIC)

http://www.aphis.usda.gov/animal_health/area_offices/
 - State
 - State veterinarian

<http://www.usaha.org/StateAnimalHealthOfficials.pdf>
- Quarantine

If you suspect a case of BSE, state or federal authorities should be notified immediately. Animals suspected with BSE should be isolated, and the farm should be quarantined until definitive diagnosis is determined.

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Recommended Actions

- Submit brain, medulla
 - Incinerate the carcass
- Quarantine the premises
- Confirmatory diagnosis
- Depopulation and trace backs
 - Proper disposal of suspect animals

Due to the serious economic and human repercussions of this disease, authorities should be notified immediately of any suspicious cases of BSE. Meat from the animal should never enter the human food chain, the brain and medulla should be submitted for necropsy, and the carcass should be 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.

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Disinfection

- Porous load autoclaving
- Sodium hypochlorite
- 2-N sodium hydroxide
- Rendering at high temperature and pressure
- Resistant in tissues, dried organic material, high titer



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. Also, prions can bind tightly to some surfaces, including stainless steel and plastic, without losing infectivity; prions bound to metal seem highly resistant to contamination. Equipment used for brain and spinal cord surgery in the U.K. is disposable for this reason.

(Information obtained from the OIE website at http://www.oie.int/eng/maladies/fiches/a_B115.htm)

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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
 - For more information, see FDA website

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, the 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

<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/BloodSafety/ucm095138.htm>)

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Additional Resources

- World Organization for Animal Health (OIE)
 - www.oie.int
- U.S. Department of Agriculture (USDA)
 - www.aphis.usda.gov
- Center for Food Security and Public Health
 - www.cfsph.iastate.edu
- USAHA Foreign Animal Diseases ("The Gray Book")
 - www.usaha.org/pubs/fad.pdf

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