

BSE: Just the Facts

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What is BSE?

Bovine spongiform encephalopathy (BSE), commonly called “mad cow disease,” is a sub-acute neurodegenerative transmissible spongiform encephalopathy (TSE) first diagnosed and described in Great Britain in November 1986 as an entirely new disease entity in cattle. The disease belongs to a group of other TSEs in animals and man that are always fatal. It is important to note that no endogenous cases of BSE have been reported outside of Europe. The United States and Canada are both free of BSE.

What are the other TSEs?

In animals, they are scrapie (sheep and goats), chronic wasting disease (deer and elk), transmissible

mink encephalopathy, and feline spongiform encephalopathy (domestic cats).

In humans, they are Creutzfeldt-Jakob disease (CJD), kuru (restricted to Papua New Guinea), Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia, and variant (v)-CJD (first identified in the United Kingdom (UK) as a result of transmission of the BSE infectious agent to humans).

What is the cause of BSE?

The cause of BSE continues to be debated in research and academic circles and remains to be fully validated and accepted universally. The compelling consensus is that the disease is caused by a prion, a rather novel addition to the world of pathogens, and not typical of

infectious agents. It (the prion) was first described by Stanley Prusiner of the University of California, San Francisco, who was awarded the Nobel Prize in Medicine in 1997 for his work.

What is a prion?

A prion or the prion protein (PrP) is a normal cell protein found on nerve cell membranes, therefore, a natural component of nervous tissue. Its finding and original description by Prusiner and associates is the result of extensive research in TSEs, prototyped by attempts to find the cause of scrapie. Since the infectious agent of scrapie possessed unusual and defying characteristics, especially its resistance to reagents such as formalin and ionizing radiation, thus

U.S. BSE Prevention Strategies

No BSE exists in U.S. cattle herds. The graphic below details the “firewall strategy” used by the U.S. government and feed, rendering, cattle, and meat industries to ensure that cattle herds remain BSE free.

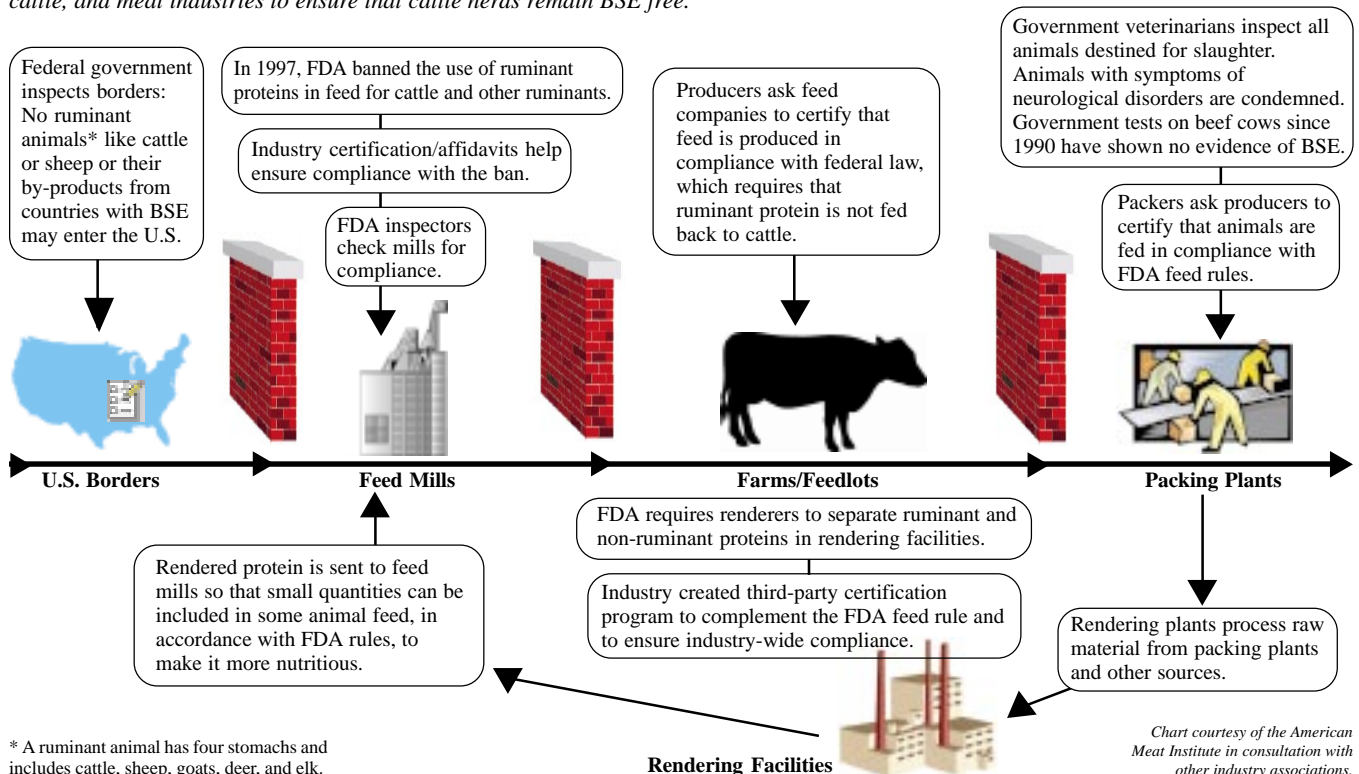


Chart courtesy of the American Meat Institute in consultation with other industry associations.

casting doubt on the long held hypothesis that the disease (scrapie) was caused by a virus, even a non-conventional or “slow” virus. This, then, provided the needed impetus for the ultimate discovery of the prion as the likely causative agent of BSE, and all TSEs, for that matter.

What are the properties of the prion?

1. Prions, like viruses, “multiply” but their properties, structures, and modes of replication appear to be basically different.
2. Unlike viruses, prions contain little or no nucleic acid.
3. Resistance to physical and chemical treatments that inactivate conventional viruses, e.g., formalin and ionizing radiation (they retain infectivity for many months in 10-12 percent formalin).
4. No evidence of an immune or inflammatory response.
5. Presence of an amyloid protein, scrapie-associated fibril.
6. They tolerate a wide range of pH, between 2.5 to 10.5.
7. They are resistant to the action of several enzymes.

How does the prion cause disease?

Every disease producing infectious organism prior to the advent of prions followed certain basic “rules” in the transmission of disease. They were dependent on nucleic acid for reproduction. The prion, however, can be considered an unconventional infectious agent and does not conform to the traditions of microbiology and disease transmission as exemplified by the bacteria, viruses, and other infectious agents. In essence, we must try to understand the prion concept with an open mind, since it is still being debated in spite of convincing evidence of its role in TSEs.

The brain makes normal PrP, in actuality, continuously; however, the normal PrP sometimes changes to a disease form and all prion diseases appear to be diseases of protein folding and protein interaction. In essence, the formation of PrP or protease-resistant protein is nothing more than a folding of the normal protein in a different or abnormal pattern, theorizing that the infectious agent of BSE (and all other TSEs) is

an abnormal protein. In most of the prion diseases, protease-resistant PrP can be demonstrated either by immunohistochemical identification of PrP amyloid or by immunoblotting of brain homogenates.

What are the main characteristics of the TSEs or prion diseases?

1. Slow, fatal, transmissible diseases of the central nervous system.
2. Occur in a variety of mammals including humans.
3. They can be experimentally transmitted to rodents.
4. After the initial “infection,” the disease can take from months to decades to appear.
5. “Infections” can occur from inoculation or ingestion (the proposed hypothesis suggesting the origin of BSE in the UK was likely a feed-borne contamination associated with the inclusion of meat and bone meal in cattle rations, possibly carrying the scrapie infectious agent).
6. The TSEs are always fatal and there is currently no sensitive pre-clinical diagnostic test available or effective treatment for any of the diseases.
7. The exact nature of the infectious agent remains unclear and in need of “final” validation beyond the prevailing consensus that it is a prion.
8. It is very possible that a co-factor may be associated with all prion diseases.

Are there differences between scrapie and BSE in the distribution of infectivity, i.e., the lesions affected, or do sheep and cattle manifest in a similar manner?

The most important aspect of scrapie in sheep and BSE in cattle is that they are both prion diseases. In spite of that significant factor, there are many distinct differences. Scrapie, since it was first clinically described in the early 1700s, has been used as the prototype of the TSEs in research, and in making comparisons with the other evolving encephalopathies. But, there are other distinct differences. In naturally infected sheep with scrapie, the infectious agent is found early in the lymphoreticular system (lymph nodes, spleen, tonsils), nasal mucosa,

and intestine; later in the central nervous system (brain and spinal cord) and placenta. Outside of the dorsal ileum in cattle with BSE, the distribution of infection is in nervous tissue (caudal medulla, spinal cord, dorsal root ganglia, trigeminal ganglia, and the frontal cortex).

Scrapie has never been proven to be associated with disease causation in humans while there is compelling epidemiological and research evidence that BSE has a linkage to v-CJD first described in the UK in 1996. Research evidence also indicates that the infectious agent of scrapie and BSE is not the same.

What is the U.S. Department of Agriculture (USDA) doing about controlling scrapie?

The Animal and Plant Health Inspection Service, USDA, is actively pursuing a Scrapie Eradication Uniform Methods and Rules (UMR) as cooperative procedures and standards with consistent states for controlling and eradicating scrapie. The UMR provides the minimum program standards and procedures for the Cooperative State-Federal-Industry Scrapie Program. The rule is established to prevent, monitor, control, and eradicate scrapie from domestic sheep and goat flocks, and for maintenance of state status in the department’s scrapie eradication program.

This is a positive approach because of the inferences of risk associated with scrapie and the analogy that scrapie may have been a likely contributing factor in the transmission and amplification of BSE in the UK.

What is the origin of BSE?

The origin or why the disease first appeared in the UK, from a standpoint of genesis, will likely never be known. A very compelling theory, albeit, still a hypothesis, is that the inclusion of meat and bone meal (MBM) from other ruminant processed raw material, with a predominant suggestion that sheep scrapie was a likely factor has been theorized. To date there have been over 180,000

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cases in the UK and about 1,400 cases elsewhere in the European Union. This equates to over 99 percent of all cases being reported in the UK.

The disease's incidence continues to fall rapidly in the UK due to stringent controls to combat the disease. In a number of other member states in the "Union," the disease has shown a sharp increase causing anxiety in the public sector and among government disease control officials.

What are the symptoms of BSE?

There is considerable variation in the clinical signs exhibited by cattle. In some instances, the first indication that an animal is affected is observed by the herdsman who notices evidence of changes in behavior exhibited as apprehension and nervousness, especially around doorways. Frenzy is often displayed with changes in sensation and marked sensitivity to touch and noise. Abnormalities of posture and movement, especially low head carriage, hind limb ataxia (failure of muscular coordination), tremors, and falling heighten the late neurological signs of the disease.

Affected animals have a tendency to lose weight and milk yield is reduced.

These signs vary in duration from one to two weeks, but quite often are prolonged up to two months. The signs are always progressive and end in recumbency (lying down) and death.

Do cattle in the United States have BSE?

All epidemiological findings to the present, based on extensive surveillance and monitoring including extensive laboratory testing, indicate that the disease does not exist in the United States. In effect, the disease is recognized as a foreign animal disease.

It is interesting to note that we have been feeding MBM in the United States for close to one hundred years without any evidence of BSE. Since MBM was suggested to be the most likely cause by British epidemiologists, why have we not seen the disease in U.S. cattle?

What about Canada?

Like the United States, Canada implemented controls that closely parallel the United States because of the close working relationship that evolves when sharing "invisible" borders. And, the country is also free of BSE based on all the current testing and epidemiology.

Does the rendering industry in the UK have an explanation for the inference or suggested hypothesis that MBM was the factor in transmitting BSE? Several theories have resulted over the years, many associated with point-counter-point and lacking in consensus. Some suggestions that have consistently been mentioned as likely contributory are: a marked increase in the total UK sheep population in the late 1970s and early 1980s with a concurrent high incidence of scrapie and the subsequent use of meat and bone meal using infected sheep tissue in the raw material stream for processing; changes from batch cookers to mainly continuous cookers in the rendering process involved lowering of the processing temperatures and a potential for resistance of the infectious agent (scrapie) to the lowered processing temperature; a discontinuation of the use of solvents for fat extraction caused a decrease in processing time and the inference that together with the lower processing temperature of continuous cooking and a lessening of the time due to the non-use of solvents, the two combined factors were considerable likely causes.

The aforementioned changes are obviously coincidental and devoid of finite proof. There are, however, other husbandry and feeding practices that should be considered contextual to likely cause relevance of BSE in the UK. There is a tendency, due to limited vegetable protein supplements like soybean and corn, to include MBM at relatively higher inclusion rates in feed rations in the UK and also feeding to calves plenty younger than is customary in the United States and most other countries. Also, if the sheep scrapie assumption is indeed valid, the amount of sheep in the rendering stream would be higher than any other country in the world, except possibly Australia and New Zealand

and both these countries are considered scrapie-free.

What is Creutzfeldt-Jakob Disease (CJD)?

CJD is the most common of the TSEs seen in humans and for reasons not fully understood occurs at the rate of one case per million in countries that compile and study health and disease statistics, including the United States. It is considered classical CJD. It is a rapidly progressive fatal disease in which nearly half the affected patients die within six months of clinical manifestations of disease. Most patients develop the disease between 55 and 70 years old, showing signs of memory loss, difficulty in walking, visual disturbances, and tremors.

The disease occurs in three main forms: 1. Sporadic, affecting about 85 percent of cases with no proven pattern of disease transmission of the affected patients, in reality, the disease just appears; 2. Familial, occurs in about five to 10 percent of CJD patients and there is normally a family history and evidence of a genetic association; 3. Iatrogenic (induced by treatment) and has been reported mainly among persons who have received growth hormone therapy derived from the pituitary gland, or dura mater, and corneal grafts.

What does CJD have to do with BSE?

Classical CJD has nothing to do with BSE and the consumption of meat, even in the UK and other countries that have BSE in their cattle herds.

What then is the association of BSE with CJD?

The association of BSE with CJD involves a hypothesis that originated in the UK and defined by the Spongiform Encephalopathy Advisory Committee (SEAC) based on an interesting and unusual cluster of 10 cases in unusually young patients with CJD that appeared as a distinct clinical entity with unique symptoms and pathology. The age at onset in the initial 10 cases ranged from 16 to 39 years with an atypically prolonged clinical course that varied from 7.5 to

22.5 months with a median of 12 months.

Some of the features of this new syndrome resembled kuru (a TSE that was limited to the Highlands of Papua New Guinea). This finding was indicative that we were dealing with another challenging syndrome within the world of the transmissible encephalopathies.

If these cases, however, as postulated, were a result of transmission of BSE to humans, as seems most likely, but still not firmly validated scientifically, it is still unclear why they should be limited to this age group. Equally troubling is why none of these cases had a pattern or history of unusual occupational or dietary exposure to the infectious agent of BSE through consumption of meat that could contain brain, spinal cord, or other nervous tissue that predominantly harbor the agent of infection.

Regardless of the debate, this unique new disease called v-CJD is the TSE that is currently associated with BSE. The debate as to the linkage and other related factors will continue because of the obvious complexity of the TSEs, but the association appears to be scientifically sound and reasonable.

Is the linkage of BSE and v-CJD really convincing, or is it just another of the hypotheses?

V-CJD, after a careful assessment and evaluation, seems to clearly represent the genesis of a new form of prion disease in the UK. A review of the epidemiology would clearly demonstrate that the statistical probability of such cases occurring randomly or by chance was exceedingly small and ascertainment bias was very unlikely as an explanation. It was becoming increasingly convincing that a new risk factor, BSE, had emerged and seemed specific for the UK and the possible causation of v-CJD.

Another significant aspect was that the disease has never appeared in any other country hitherto, and only in a country with reported BSE. The same can affirm other episodes of the disease that have occurred in both France and Northern Ireland, both

countries also reporting BSE in their cattle herds, and concurrently v-CJD.

Research findings have also strongly affirmed the likely linkage of BSE and v-CJD.

How safe is U.S. beef supply?

Our regulatory infrastructure has built numerous “firewalls” including protection of our borders by restricting imports from at-risk countries, active surveillance at different levels from slaughterhouses to on-farm monitoring and testing, and the control of feeding cattle prohibited protein (the “feed ban”). The safety of our beef supply can be best highlighted by a comment of Dr. George Gray, Harvard University epidemiologist: “We have systems in place that, if they work properly, should keep “mad cow” out of our country. Even if the disease were to occur here, the risk to people is low because of the many safeguards in place to detect a sick animal so it couldn’t be eaten.” And, for the record, the infectious agent has not been detected in the muscle tissue that is usually eaten by consumers of beef.

In essence, U.S. beef is as safe as we can possibly make it.

What about milk and other dairy products from the cattle industry?

There is no evidence to date that the infectious agent or prion is transmitted through milk or any dairy products for that matter. The infectious agent in cattle is predominantly limited to the brain, spinal cord, and in general nervous tissues. In the early stages, the distal ileum is involved. This has been substantiated by the World Health Organization that defined risk in a worst case scenario by stating that milk and other dairy products made from milk, even in countries with a high incidence of BSE, can be safely consumed.

Then, why the media hype about BSE and the likely risk in the United States?

Perception of risk and the danger associated with potential hazards is linked to knowledge. The overall understanding of the TSEs by the public is very low, because not only

does the public have a low comprehension of science in general, but the complexity of the prion diseases defies easy answers. Information, therefore, is not readily disseminated in a format that is explicit and perception becomes reality.

What is the rendering industry doing as part of the BSE control initiative?

The rendering industry long before any regulatory controls were instituted in both the United States and Canada took voluntary proactive measures based on the existing information at the time by excluding sheep (one year or older) from entering the rendering stream. That policy was implemented in 1989 and remains a practice continued today by many rendering companies because of the inference made by British epidemiologists that rendered sheep raw material included in the production of MBM was a likely associative link in the transmission of BSE in the UK.

Since that initial voluntary program, the industry has worked closely with other livestock and agricultural coalitions and collaborated in efforts to be part of the “firewall” to prevent any possible amplification of the infectious agent through feed to cattle. The industry also worked cooperatively with the Food and Drug Administration (FDA) in the formulation of the rule that became effective August 4, 1997, “Animal Proteins Prohibited From Use in Ruminant Feed,” Title 21, Code of Federal Regulations, Part 589.2000.

Additionally, on April 1, 2001, the Animal Protein Producers Industry, the biosecurity arm of the rendering industry, established an inspection audit of all animal protein producers to ascertain compliance with the FDA rule through an independent third party audit performed by a nationally respected firm of auditors, Cook & Thurber of Madison, WI. ♦

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