BOVINE SPONGIFORM ENCEPHALOPATHY (BSE)

Animal Group(s) Affected	Transmission	Clinical Signs	Severity	Treatment	Prevention and Control	Zoonotic
Naturally affected: Cattle - *Bos taurus* and *B. indicus*; captive exotic ungulates of Bovidae; felines both domestic and captive exotic; domestic goats.	Ingestion of BSE contaminated feed (i.e., meat and bone meal) or infected carcasses.	Apprehension, nervousness and/or aggression; tremoring, incoordination, especially hind-limb ataxia and difficulty in rising; hyperesthesia.	Average incubation period is 2-8 years. The clinical duration is usually several weeks to 6 months. The disease is invariably progressive and fatal.	None.	Prohibit the feeding of most ruminant or mammalian proteins to ruminants.	Yes.

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Susceptible animal groups: Ruminants such as cattle (*Bos taurus* and *B. indicus*), sheep and goats, captive exotic ungulates (eland, gemsbok, Arabian and scimitar-horned oryx, nyala and greater kudu) and American bison (*Bison bison*). Felines both domestic cats and captive exotic cats (cheetah, lion, Asian leopard cat, ocelot, puma and tiger) have been reported as "Feline Spongiform Encephalopathy (FSE)". Experimentally, non-human primates also have been infected via the oral and intracranial routes.

Causative organism: The etiological agent has not been fully characterized. Understanding of the causative agent remains imperfect, but a wealth of accumulating evidence has led to the conclusions that: (i) a misfolded form of the protein (PrP^{TSE}), known as a prion, acts as a template to induce normal protein molecules to cascade into the same misfolded configuration; (ii) infectivity is associated with an aggregate (or polymer) of 14-28 misfolded protein molecules; (iii) an as yet unidentified host molecule (?chaperone, ganglioside, non-coding RNA) is probably necessary as a cofactor in replication; (iv) the degree of similarity in the primary structure of the protein in different species influences the ease with which the protein can induce inter-species disease; and (v) in some species, the entire process appears to occur spontaneously in the sporadic form of disease, but can be initiated (i.e., 'transmitted') by the introduction of tissue from a diseased to a healthy host, as would have happened when humans consumed BSE-contaminated meat products. Until 2004, it appeared that a single "strain" caused all cases of BSE. It is now known that there are at least two additional strains called L-Type and H-Type atypical BSE.

Little is known about atypical BSE. The origin and natural routes of transmission, if any, have yet to be determined. Almost all cases have been in older cattle (usually > 8 years of age) that have shown little resemblance to the clinic-pathological picture seen in classical disease. It has been suggested that the disease may be sporadic or be caused by a genetic mutation, but no convincing evidence has been found to support either of these ideas. The correct answer will probably only come by study of the future annual incidence curves of both types of disease. Regardless of the origin of atypical BSE, the possibility of recycling the disease in cattle and other ruminants, as well as the potential for transmission to humans, mandate a

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continuation of feed and specified-risk materials (SRM) bans, together with diagnostic testing programs for some time to come.

Zoonotic potential: BSE is the cause of the fatal human disease, variant Creutzfeldt-Jakob Disease (vCJD). Epidemiological evidence indicates that transmission is through the consumption of meat products contaminated with BSE agent, which is found primarily in CNS tissue and distal ileum. During the incubation period, it appears that humans may transmit vCJD to other humans via blood transfusions.

Distribution: The first cases of BSE were recognized in the United Kingdom in 1986 and because of recycling of offals into animal feed, the disease rapidly became epidemic in the UK and spread to most other European countries via the trade of contaminated meat and bone meal and infected animals that entered slaughter channels. Worldwide, the number of cases at the end of 2012 was approximately 190,000, all but 6,000 of which were within the UK. In addition to the officially reported and confirmed cases, it is estimated that as many as 3.5 million animals were infected and may have entered the food and feed chains in the UK without being detected. BSE has also been detected in Brazil (atypical), Canada, Falkland Islands (import), Israel, Japan, Oman (import) and the US (import and atypical). Implementation of feed controls has all but eliminated classical BSE, as there were only 21 total cases reported worldwide in 2012. This number includes both classical and atypical BSE. The UK found only 3 cases in 2012. Statistics regarding the occurrence of BSE may be found at http://www.oie.int/en/animal-health-in-the-world/bse-specific-data/. It should also be noted that the absence of reported cases over an extended time in a country might not indicate so much the absence of disease as a lack of adequate surveillance.

Naturally occurring cases of BSE in species other than cattle have been very limited and have been linked to exposure to contaminated feed or infected carcasses. The majority of cases originated in the UK and like BSE in cattle, have declined with the implementation of feed controls. None of the exotic animals were infected in the wild.

Incubation period: The incubation period for BSE is measured in years and in cattle can range from 2-8 years.

Clinical signs: Affected animals develop a progressive degeneration of the nervous system. They may display changes in temperament, abnormalities of posture and movement, and changes in sensation, including signs of apprehension, nervousness or aggression, incoordination, especially hind-limb ataxia, tremor and difficulty in rising, and hyperesthesia to sound and touch. In addition, many animals have decreased milk production and loss of body condition despite continued appetite. Only a small proportion of affected cattle exhibit what would be considered typical "mad cow" signs. BSE can be mistaken for other conditions or go unnoticed due to subtlety of the signs. The TSE cases in exotic ruminants had a younger onset age and a shorter clinical duration compared to that in cattle with BSE. Clinical signs in the exotic ungulates are similar to those seen in cattle and include ataxia and wasting.

FSE is characterized by progressive nervous signs, including ataxia, hyper-reactivity and behavioral changes and is fatal.

Clinical pathological, gross, and histopathological findings: No gross pathological lesions are found in animals affected with BSE and histological changes appear to be confined to the CNS. The primary lesions found are non-inflammatory vacuolation of neuronal perikarya and grey-matter neuropil and are usually bilaterally symmetric. Astrocytosis may also be observed. Infected animals may not manifest these lesions until end stage disease. Histological changes that are seen in cattle are similar to those seen in the other affected animal species.

Diagnosis: No live animal test for BSE is available. Historically, the diagnosis of BSE relied on the occurrence of clinical signs of the disease confirmed by postmortem histopathological examination of brain tissue. The current diagnostic tests target the detection of PrP^{TSE} (the misfolded form of the prion protein)

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deposits in the CNS. Immunohistochemistry and/or Western blots are usually used as confirmatory tests. In addition, a number of rapid immunoassays have been developed and approved by governments for use as screening tests. These include enzyme-linked immunosorbent assays (ELISAs), automated immunoblotting (Western blotting) and lateral flow devices (LFD).

Material required for laboratory analysis: Clinically suspect cases should be subjected to a standard neuropathological approach in which the whole brain is sampled, and a range of representative areas examined. BSE sampling is dependent upon the test methods approved and used by the national veterinary services. For example, in the US brain stem, including the obex, should be submitted as fresh tissue. Countries using immunohistochemistry as the primary diagnostic test may require samples submitted in formalin.

Relevant diagnostic laboratories:
USDA-APHIS
National Veterinary Services Laboratory
1920 Dayton Ave. (for packages)
P.O. Box 844 (for letters)
Ames, IA 50010
(515) 337-7266
Fax: (515) 337-7397

Treatment: None

Prevention and control: Given that the primary, if not sole, route of BSE transmission is through the feeding of contaminated meat-and bone-meal (MBM) to cattle, countries with any risk factors need to implement feed controls. The level of restriction is usually dependent upon the amount of contamination thought to be in the system. Three main factors can increase the stability of a national feed production system:

(i) Feed bans – these regulations can range from the basic prohibition of feeding ruminant MBM back to ruminants; to prohibiting most animal proteins from being fed to all animals used for food production, including fish.

(ii) Specified Risk Materials (SRMs) ban – this ban requires that high infectivity tissues such as bovine brain and spinal cord be removed from both the food and feed chain and be destroyed. The intent of this control is to remove the primary source of infectivity from the entire system to prevent the possibility of cross-contamination.

(iii) Regulation of rendering – although no rendering process can completely remove all detectable infectivity, some are more effective than others. The best procedure identified to date requires 133°C at 3 bars of pressure for 20 minutes.

Experience in countries that have spent considerable effort to eliminate BSE has underlined the need for an extremely high level of compliance with feed controls in order to remove the agent from the system and prevent new infections in cattle. No complacency can be tolerated.

Bovine products and byproducts are widely used for both food and pharmaceuticals, and hence require the highest level of safety. Because of the hardy nature of the BSE agent and its high potential for cross-contamination, the most effective approach to protect bovine products and bovine-derived materials for human use from contamination by BSE is to ensure that infected animals or carcasses never enter processing plants. Because there are presently no diagnostic tools sensitive enough for detection of the disease during its long preclinical incubation, governments must rely on measures to prevent exposure through feed (see above) or prohibit high risk tissues (SRMs) from being used for food or pharmaceuticals.

Suggested disinfectants: BSE is not known to spread laterally between cattle or other animals; hence it is not

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necessary to disinfect a premise where infected cattle have been. Regarding BSE, the need for disinfection may arise in diagnostic laboratories, food processing and pharmaceutical manufacturing plants. The agent of BSE shares with other TSE agents the property of unusual resistance to destruction. None of the standard disinfection methods is effective, including irradiation or exposure to various chemical disinfectants. Even harsher conditions that are capable of inactivating all other known pathogens (including bacterial spores), such as heating under pressure at 121°C, exposure to dry heat at 600°C, or immersion in 0.1 N NaOH or 0.5% bleach cannot assure complete inactivation. Currently, the only procedures known to completely eliminate detectable infectivity are exposure to dry heat at 1000°C, immersion in either 1 N NaOH or fresh undiluted bleach, and steam heating under pressure at 132°C. The preferred method is a sequential exposure to both NaOH and steam autoclaving inactivation treatments.

Notification: BSE is a reportable disease in the US.

Measures required for introducing animals to infected animal: This approach is not applicable.

Conditions for restoring disease-free status after an outbreak:

As BSE is not known to be laterally transmitted, no remediation for farms or zones within a country is needed. After a case of BSE has been detected within a country, certain measures must be taken to regain negligible risk status. As per the World Organization for Animal Health (OIE), countries detecting BSE must perform a risk assessment to identify historical and existing risk factors. The country must demonstrate that appropriate specific measures have been taken for the relevant period of time defined below to manage each identified risk.

EITHER:

a) If there has been a case, every case of BSE has been demonstrated to have been imported and has been completely destroyed, and it has been demonstrated through an appropriate level of control and audit, including that of cross contamination, that for at least eight years neither meat-and-bone meal nor greaves derived from ruminants has been fed to ruminants;

OR:

b) If there has been an indigenous case, every indigenous case was born more than 11 years ago; and the below points have been complied with for 7 years.

- An education program is in place for those involved in the livestock industry to report all suspected cases of BSE.
- BSE is reportable and all suspect cases are investigated.
- Diagnostics are carried out in accordance with the OIE laboratory manual.

AND:

i) it has been demonstrated through an appropriate level of control and audit, including that of cross contamination, that for at least eight years neither meat-and-bone meal nor greaves derived from ruminants has been fed to ruminants.

ii) All BSE cases, as well as:

- all cattle which, during their first year of life, were reared with the BSE cases during their first year of life, and which investigation showed consumed the same potentially contaminated feed during that period, or
- if the results of the investigation are inconclusive, all cattle born in the same herd as, and within 12 months of the birth of, the BSE cases if alive in the country, zone or compartment, are permanently identified, and their movements controlled, and, when slaughtered or at death, are completely destroyed.

Experts who may be consulted:

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