

Bovine Spongiform Encephalopathy

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Synonym: Mad Cow Disease

Importance

Bovine spongiform encephalopathy (BSE, “mad cow disease”) is a type of transmissible spongiform encephalopathy (TSE) that affects cattle. TSEs are progressive and fatal neurodegenerative diseases. There are multiple TSEs which affect different species of animals including scrapie in sheep, transmissible mink encephalopathy (TME, mink scrapie), feline spongiform encephalopathy (FSE), chronic wasting disease (CWD) in deer, and a spongiform encephalopathy of exotic ruminants. These diseases were once thought to be entirely species specific, but it now appears that some agents can cross species barriers. In the United Kingdom, factors leading to the BSE epidemic may have been responsible for concurrent outbreaks of FSE in cats and spongiform encephalopathy in exotic ruminants. BSE has also been linked to a variant of Creutzfeldt-Jakob disease (CJD) in humans.

Etiology

BSE is thought to be caused by prions, a proteinaceous infectious particle that is smaller than the smallest known virus. Prions have not been completely characterized and a minority opinion is that BSE may be caused by virinos or retroviruses. The BSE agent is extremely resistant to the treatments that ordinarily destroy bacteria, spores, viruses, and fungi and can survive in tissue post-mortem.

Species affected

BSE is seen in cattle and can be experimentally transmitted to cats, mink, mice, pigs, sheep, goats, marmosets and cynomolgus monkeys.

Geographic distribution

BSE appears to have originated in the United Kingdom in 1986. Infected indigenous cattle have since been found in Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Israel, Italy, Japan, Lichtenstein, Luxembourg, Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Switzerland, United Kingdom and Canada. Cases have also been seen in imported cattle in Oman, Liechtenstein, Luxembourg, and the Falkland Islands.

BSE has never been detected in Australia, New Zealand, the United States or South America.

Transmission

BSE seems to be transmitted orally and is thought to have mutated from the scrapie agent found in sheep. The first cases of BSE appeared in the U.K. in 1986 and have been linked to changes in the rendering practices for livestock feed. These changes may have allowed infectious meat or bone meal from scrapie-infected sheep to be fed to cattle. Rendering of contaminated cattle carcasses and wastes seems to have amplified the agent. A minority of researchers believes that BSE has always existed in cattle but was unrecognized until the outbreak in the U.K.

The BSE agent is found mainly in nervous tissues. In naturally infected cattle, it has been detected only in the brain, spinal cord, and retina. In experimentally infected calves, it is also seen in the distal ileum. This agent has never been found in muscle, blood, or milk, and natural infections do not seem to spread

laterally between cattle. The offspring of BSE-infected cattle have an increased risk of developing BSE, but it is not known whether this is due to vertical transmission or another mode of transmission.

Incubation period

All TSEs have incubation periods of months or years. The incubation period of BSE is more than a year and often several years. The peak incidence of disease occurs in 4 to 5 year old cattle.

Clinical signs

Bovine spongiform encephalopathy is usually insidious in onset and tends to progress slowly. The clinical signs are neurologic and once the symptoms appear, the diseases are relentlessly progressive and fatal. The clinical signs of BSE may include hyperesthesia, hindlimb ataxia, pelvic swaying, hypermetria, tremors, falling, and behavioral changes such as apprehension, nervousness, and occasionally frenzy. Intense pruritus is not usually seen. Nonspecific symptoms include loss of condition, weight loss, and decreased milk production. Decreased rumination, bradycardia, and altered heart rhythms have also been reported. The disease progresses to recumbency and coma, and death occurs from weeks to months later. Rare cases may develop acutely and progress rapidly within days.

Post mortem lesions

The only gross lesions found include emaciation or wasting of the carcass in some cases. The typical histopathologic lesions are confined to the central nervous system. Neuronal vacuolation and non-inflammatory spongiform changes in the gray matter are pathognomonic. Amyloid plaques are rarely seen in BSE cases. Lesions are usually but not always bilaterally symmetrical.

Morbidity and mortality

BSE is always fatal once the symptoms appear. In 1992, the annual incidence of BSE in United Kingdom cattle was 1%; however, the number of cases has been decreasing in recent years.

Diagnosis

Clinical

BSE should be suspected in animals that develop a slowly progressive, fatal neurologic disease.

Differential Diagnosis

The differential diagnosis of BSE includes nervous ketosis, hypomagnesemia, listeriosis, polio, rabies, brain tumor, spinal cord trauma, and lead poisoning.

Laboratory Tests

BSE is diagnosed by histopathology. A diagnosis can also be made by detecting PrP^{Sc} (a disease-specific isoform of the membrane protein PrP) in the central nervous system. Accumulations of PrP^{Sc} can be found in unfixed brain extracts by immunoblotting and in fixed brains by immunohistochemistry. The diagnosis can also be confirmed by finding characteristic fibrils of PrP^{Sc} (scrapie-associated fibrils) with electron microscopy in brain extracts. Some of these tests can be used on frozen or autolyzed brains. BSE can be detected by transmission studies in mice. However, an incubation period of several months often makes this technique impractical for diagnosis. New commercial tests to detect BSE (PrP^{Sc}) in cattle brain samples include a modified immunoblot, a chemiluminescent ELISA test, a sandwich immunoassay, and a two-site noncompetitive immunometric procedure. Serology is not useful for diagnosis, as antibodies are not made against the BSE agent.

Samples to collect

Before collecting or sending any samples from animals with a suspected foreign animal disease, 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. A fatal human encephalopathy (vCJD) has been linked to BSE; samples should be collected and handled with all appropriate precautions.

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 detection, cervical spinal cord or caudal medulla should be extracted and frozen soon after death. During epidemics of BSE, it may be possible to remove only the hindbrain via the foramen magnum for disease monitoring.

Recommended action if BSE is suspected

Notification of authorities

BSE is an exotic disease and authorities must be notified immediately of any suspicious cases. Federal Area Veterinarian in Charge (AVIC) www.aphis.usda.gov/vs/area_offices State veterinarian <http://aphis.usda.gov/vs/sregs/official/html>

Quarantine and disinfection

BSE does not appear to spread laterally, but once an animal is found positive the whole herd is quarantined and trace backs will occur. The prototype agent, scrapie, is highly resistant to disinfectants, heat, ultraviolet radiation, ionizing radiation, and formalin, especially if it is in tissues, dried organic material or at a very high titer. Effective disinfection is possible with a single porous load autoclave cycle of 134-138°C for 18 minutes. Infectious tissues should either be autoclaved under the same conditions or incinerated. Sodium hypochlorite and sodium hydroxide are effective chemical disinfectants; sodium hypochlorite containing 2% available chlorine or 2-N sodium hydroxide should be applied for more than 1 hour at 20°C and overnight for equipment. Rendering at 133°C at 3 bar pressure for a minimum of 20 minutes is used in Great Britain in order to dispose of the infected carcasses. Many medical experts recommend the use of disposable instruments in neurosurgery if the risk of contacting highly infective CJD tissue is high. Equipment used for brain biopsies in the U.K. is quarantined until a diagnosis is confirmed because risk of CJD spread is too high to try and disinfect to reuse those instruments.

Public health aspects

Current thinking is that people who ingest BSE contaminated food products may develop variant Creutzfeldt Jakob Disease (vCJD). The incubation period for vCJD is unknown because it is a relatively new disease, but it is likely that it is 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, 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. 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 includes 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. There is no known effective treatment for vCJD though there is experimental treatment taking place with Quinidine. Supportive treatment and symptomatic care are recommended. From 1995 (when the first suspected cases of vCJD occurred) to July 2003, 132 cases of vCJD have been reported in the U.K. There has been no confirmed case of vCJD originating in the United States. The peak incidence of BSE cases occurred in January 1993 with 1,000 new cases every week.

For more information

World Organization for Animal Health (OIE)
<http://www.oie.int>

OIE Manual of Standards
http://www.oie.int/eng/normes/mmanual/a_summry.htm

United States Department of Agriculture Animal and Plant Health Inspection Service

<http://www.aphis.usda.gov/>

Canadian Food Inspection Agency

<http://www.inspection.gc.ca/english/anima/heasan/disemala/disemalae.htm>

Animal Health Australia. The National Animal Health Information System

<http://www.aahc.com.au/nahis/disease/dislist.asp>

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