



BSE Backgrounder

(1/05/04)

Causative agent

Bovine spongiform encephalopathy (BSE), commonly referred to as “mad cow disease,” belongs to the family of diseases known as transmissible spongiform encephalopathies (TSE). The causative agent of BSE has not been fully characterized, but three possibilities have been proposed: an unconventional virus, a prion (a self-replicating protein), or a virino (incomplete virus) comprising naked nucleic acid protected by host proteins. The theory accepted by most scientists is that BSE is caused by a prion. The agent does not invoke a detectable immune response or inflammatory reaction in its host and is extremely resistant to sterilization processes.

Natural distribution

A chronic, degenerative neurologic disease of cattle, BSE has been diagnosed in native-born cattle in Austria, Belgium, Canada, the Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Israel, Italy, Japan, Liechtenstein, Luxembourg, the Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Switzerland, and the United Kingdom. More than 95% of cases identified have developed in the United Kingdom. A single case of BSE was confirmed in the United States in December 2003. The origin and circumstances of this case are currently being investigated. Other countries with a single case are Austria, Finland, Greece, and Israel. Canada has had one case in a native-born cow and one in an imported cow.

Transmission

Researchers believe that BSE is spread to cattle through feeding of contaminated meat and bone meal from scrapie-infected sheep or cattle with previously unidentified BSE. Offal tissues of particular risk include the brain, spinal cord, eyes, spleen, distal ileum, and certain other nervous tissues. Bovine spongiform encephalopathy does not appear to be spread horizontally (contact between cattle or contact between cattle and other TSE-affected species).

Clinical signs of BSE in cattle

In cattle, BSE causes progressive degeneration of the central nervous system. Clinical signs may include changes in temperament (e.g., apprehension, nervousness, unwillingness to move through doorways, belligerence), hyperesthesia, ptyalism, pruritis of the head, fine muscular fasciculations, moaning, tachypnea and bradycardia, incoordination, proprioceptive deficits, abnormal postures, abnormal gait, decreased milk production, loss of body condition despite a normal appetite, recumbency, and death. The incubation period ranges from 2 to 8 years and the health of affected animals typically deteriorates over a period of 2 weeks to 6 months. The disease is uniformly fatal. Most cattle affected are between 3 and 6 years old, although BSE has been diagnosed in younger and older cattle.

Diagnosis

Unfortunately, no laboratory test to confirm BSE in a live animal currently exists. Bovine spongiform encephalopathy is most often diagnosed by postmortem microscopic examination of brain and spinal cord tissue. Examination will reveal bilaterally symmetrical neuronal vacuolation and spongiform degeneration, often with hypertrophy of astrocytes. Vacuolation is greatest in the medulla oblongata; the central gray matter of the midbrain; and the paraventricular area of the hypothalamus, thalamus, and septal area.

Immunohistochemistry, immunoblotting (Western), and ELISA are used to confirm the presence of the abnormal prion protein in brain and spinal cord tissue.

Prevention

Because the primary source of transmission of BSE has been shown to be abnormal proteins derived from BSE-infected ruminants in feed, the Food and Drug Administration (FDA) has established regulations that prohibit the feeding of most mammalian proteins to ruminants in the United States. The United States Department of Agriculture's Animal and Plant Health Inspection Service (USDA-APHIS) has restricted importation of live ruminants and ruminant products (e.g., fetal bovine serum, meat-and-bone meal, bonemeal, bloodmeal, offal, fats, glands) from countries where BSE has been diagnosed. Low risk products (e.g., boneless meat from cattle younger than 30 months old) can be imported from Canada. Because of concerns about cross-contamination of rendered products of nonruminant origin with the BSE agent, since 2000 the USDA has also prohibited all imports of rendered animal protein products, regardless of species.

Treatment

No treatment currently exists for cattle affected with BSE. The disease is uniformly fatal.

Infection control

Veterinarians are trained to recognize the clinical signs and pathologic manifestations of BSE in cattle. The USDA-APHIS has distributed videotapes, fact sheets, literature reviews, and risk assessments on BSE to state and federal veterinarians, colleges of veterinary medicine, extension veterinarians, private practitioners, and producers. Veterinary diagnostic laboratories have been provided with microscope slides showing typical lesions of BSE to assist in pathologic confirmation of suspect cases.

An active interagency surveillance program, coordinated by the USDA-APHIS, collects samples from cattle exhibiting signs of neurologic disease, cattle condemned at slaughter for suspected neurologic disease, cattle for which results of rabies testing conducted at veterinary diagnostic laboratories is negative, and aged nonambulatory cattle and examines these for the presence of abnormal prions.

Cattle destined for slaughter in the United States are evaluated by the Food Safety and Inspection Service (USDA-FSIS) for signs of disease, including central nervous system impairment. Animals showing signs of systemic disease, including those exhibiting signs of neurologic impairment, are condemned and not used for human food. The USDA also prohibits tissues from nonambulatory (downer) cattle from entering the human food supply.

Transmissible Spongiform Encephalopathies in Other Animals

The family of transmissible spongiform encephalopathies (TSE) in animals includes scrapie, affecting sheep and goats; transmissible mink encephalopathy; chronic wasting disease,

affecting deer and elk; and, in humans, kuru, classic and variant Creutzfeldt-Jakob disease, Gerstmann-Straussler syndrome, and fatal familial insomnia. A neurologic disease in exotic ruminants and exotic and household cats in the United Kingdom has been linked to BSE, and is suspected to be caused by eating feed contaminated with the BSE agent.

Implications of BSE for Humans

Variant Creutzfeldt-Jakob disease (vCJD) is a transmissible spongiform encephalopathy having epidemiologic and pathologic evidence of a causal link with BSE. It primarily affects young adults (median age at death is 28 years). Symptoms include early psychiatric and sensory abnormalities, eventually followed by ataxia, dementia, and myoclonus. Median duration of illness is 14 months. Current thinking is that vCJD may be caused by ingestion of products contaminated with the BSE agent.

Tissues considered to be of greater risk (e.g., skull, brain, trigeminal ganglia, eyes, vertebral column, spinal cord, and dorsal root ganglia of cattle more than 30 months old, and the distal ileum of cattle of all ages) have been banned from entering the human food supply in the United States, Canada, and European Union. In the United States, tissues from nonambulatory (downer) cattle also may not be used for human food. Milk and milk products are not believed to pose a transmission risk, and tallow and gelatin are considered safe if they have been prepared by a manufacturing process that inactivates or removes the BSE agent.

Variant CJD must be differentiated from classic CJD, which is the TSE most often identified in humans. Classic CJD occurs worldwide at a rate of about 1 to 2 cases/1 million people. Mean age of onset is 65 years and median duration of illness is 4.5 months. Hereditary predisposition accounts for approximately 5 to 10% of cases, a sporadic form accounts for approximately 85 to 90% of cases, and a small number of cases are iatrogenic (transmitted via contaminated surgical equipment, transplants [e.g., cornea, dura mater], or administration of natural human growth hormone).