Case Definition

Bovine Spongiform Encephalopathy (BSE)
(Notifiable)

October 2024

1. **Disease Information**
   - **1.1 General Disease and Pathogen Information:** Bovine spongiform encephalopathy (BSE), widely referred to as “mad cow disease,” is a progressive and fatal neurologic disease, predominantly, of bovines. It is caused by an abnormal prion protein, which is an unconventional transmissible agent. BSE belongs to a family of diseases known as transmissible spongiform encephalopathies that includes scrapie in sheep and goats, chronic wasting disease in deer, elk and moose, and classical and variant Creutzfeldt-Jakob disease, among other syndromes in humans. The prion agent is resistant to enzymatic breakdown and most disinfection treatments. BSE, which is not contagious, exists in two forms: classical (C-type) and atypical (L- or H-type). BSE has a long incubation period, averaging 2 to 8 years in bovines. Classical BSE has peak occurrence in bovine ages 4 to 5 years. The primary source of infection for classical BSE is feed contaminated with the infectious prion agent, such as meat and bone meal containing protein derived from rendered infected bovines. Atypical forms of BSE are believed to occur spontaneously at extremely low rates in all bovine populations. Cases of atypical BSE have only been identified in older bovines through surveillance for the classical, epizootic form of BSE and are considered incidental findings. The classical BSE prion has zoonotic potential; humans have developed variant Creutzfeldt-Jakob disease after eating tissues from an infected animal containing the prion. Classical prions have been reported in some European countries, Canada, Israel, and Japan. Atypical BSE prions have been reported in Europe, the United States, Canada, Japan, and Brazil.
   - **1.2 Clinical Signs:** Clinical signs of BSE are largely nonspecific and may include gait abnormalities (especially hindlimb ataxia or a modified gait in which the legs move in lateral pairs), incoordination, difficulty navigating obstacles, low carriage of the head, hyper-responsiveness to stimuli, tremors, arched back, persistent licking or rubbing, weight loss, loss of condition, teeth grinding, decreased milk production, decreased rumination, and bradycardia. Clinical signs can also include behavioral changes like aggression, nervousness, apprehension, reluctance to being milked, pacing, or frenzy. A combination of behavioral changes plus gait abnormalities is highly suggestive of BSE but is not seen in all cases. Signs of BSE usually worsen gradually over a few weeks to several months but occasionally progress rapidly. BSE is progressive and fatal, and final stages of the disease are characterized by recumbency, coma, and death.
2. **Laboratory Criteria**
   - **2.1 Agent Isolation and Identification:** There is no method for confirming BSE in a live animal. The agent is a partially protease-resistant, misfolded isoform of a normal cellular protein, PrP^{C}. The abnormal form is variably referred to as PrP^{BSE}, PrP^{res}, or

PrP^{Sc}. Confirmation of the diagnosis is achieved by immunochemical and/or immunohistochemical detection of the abnormal prion in brain tissue, specifically the obex region of the medulla oblongata (brainstem). Rapid tests are currently the main approach for the primary detection of BSE. These tests are commercially available and allow large numbers of samples to be screened. Rapid screening tests include rapid western immunoblot, lateral flow assays, and ELISA. The relative sensitivities of rapid tests have not been fully determined as PrP^{Res} proteins are variable within the brain. Thus, rapid test should only provide a means of primary screening. Immunohistochemistry (IHC) is a confirmatory test for BSE. IHC testing examines brain samples visually using antibodies in a staining technique to demonstrate the presence of abnormal prion proteins. It is possible to test for PrP^{Res} by IHC on material that has been frozen prior to fixation. IHC examination is performed on the same formalin-fixed, paraffin-embedded material used for histopathology. Histopathologic changes suggestive of BSE can be present on examination of a single section of medulla oblongata at the level of the obex or with extensive examination of the brainstem. Examinations are carried out using the same tissue as for IHC.

2.2 Agent Characterization: Differentiating the atypical forms from classical BSE is based on Western immunoblot pattern comparison and/or bioassay characterization. Western immunoblot testing is a confirmatory test used to differentiate classical BSE from atypical forms (L- and H-type) of BSE. Immunoblotting techniques are carried out on fresh, unfixed tissue from the obex region. It can be successfully applied even when tissue is autolyzed.

2.3 Serology: No specific immune responses to BSE are detectable.

3. Case Classification

3.1 Suspect Case: Any bovine (*Bos taurus* or *Bos indicus*) with

3.1.1 clinical signs consistent with BSE; **OR**

3.1.2 an epidemiological link; **OR**

3.1.3 history consistent with BSE.

3.2 Presumptive Positive Case: A suspect case that has

3.2.1 a non-negative rapid screening test at an approved National Animal Health Laboratory Network (NAHLN) laboratory (referred to as an “initial reactor”); **AND**

3.2.2 repeat rapid screening testing of the initial reactor resulting in a second non-negative result (referred to as “inconclusive”).

3.3 Confirmed Positive Case: A presumptive positive case with the examination of central nervous system tissue via detection of PrPRes by western blot, IHC, or other World Organisation for Animal Health-recognized confirmatory test performed at National Veterinary Service Laboratories (NVSL).

4. Reporting Criteria: BSE is a U.S. Notifiable disease that is immediately reportable under the APHIS National List of Reportable Animal Diseases (NLRAD).

4.1 NLRAD reporting is in accordance with the NLRAD Standards for Notifiable diseases, and is reported by APHIS to the World Organisation for Animal Health (WOAH); **AND**

4.2 FAD or Emerging Disease Incidents (EDI) also follow standard procedures according to the Policy for the Investigation of Potential Foreign Animal Disease/Emerging Disease Incidents.