Transmissible Spongiform Encephalopathies (TSE)

TSE’s are rare forms of progressive neurodegenerative disorders that affect both humans and animals and are caused by similar uncharacterized agents that generally produce spongiform changes in the brain. Specific examples of TSE’s include: scrapie, which affects sheep and goats; bovine spongiform encephalopathy (BSE), which affects cattle; transmissible mink encephalopathy; feline spongiform encephalopathy; chronic wasting disease (CWD) of mule deer, white-tailed deer, black-tailed deer, and elk; and in humans, kuru, Creutzfeldt-Jakob disease, Gerstmann-Straussler syndrome, fatal familial insomnia, and variant Creutzfeldt-Jakob disease (vCJD).

Diagnosis: TSE’s are insidious degenerative diseases of the central nervous system. Historically, the diagnosis of TSE’s has been based on the occurrence of clinical signs of the disease, which was confirmed only by postmortem examination of brain tissue. More recently, identification of abnormal prion protein, PrPres, by various techniques has improved our ability to make a disease diagnosis.

Laboratory Testing: A characteristic feature of all TSE’s is the lack of a measurable host immune response to the agent meaning that there are no antibodies produced. No conventional serologic test can be used to identify infected animals. Scientists usually diagnose TSE diseases in the laboratory by histopathologic examination of the brain followed by one or more supplemental tests. A description of these tests is attached.

Scrapie: Scrapie was first diagnosed in the United States in 1947. Control programs have been in place since 1952. The latest program went into effect in 1992. It involves a Flock Certification Program and interstate movement regulations that place restrictions on the movement of sheep and goats from infected and source scrapie flocks. The intent of the certification program is to monitor flocks over a period of 5 years or more and identify flocks that have not displayed evidence of scrapie. Flocks are inspected yearly for compliance with the certifica-
TME: There is no official USDA program for TME. We continue to monitor for reoccurrence of TME disease. The last known case of TME occurred in the United States in 1985. There were other outbreaks prior to 1964.

Testing Methods for TSE’s

Histopathology: Bilaterally symmetrical degenerative changes are usually seen in the gray matter of the brain stem. These changes are characterized by vacuolation or microcavitation of nerve cells in the brain stem nuclei. The neural perikarya and axons of certain brain stem nuclei contain intracytoplasmic vacuoles of various sizes, giving the impression of a spongy brain. Hypertrophy of astrocytes (astrocytosis) often accompanies the vacuolation.

Electron Microscopy: A TSE diagnosis may also be made when scrapie-associated fibrils (SAF) using negative stain electron microscopy are detected.

Supplemental tests: Supplemental tests are available to enhance the diagnostic capabilities for TSE’s. Research shows the partially protease-resistant form of the prion protein (PrPres) is found in the brain of TSE-infected animals. Two tests that have been used routinely to detect PrPres in animals showing clinical signs of a TSE are immunohistochemistry and a Western-blot technique. In the past, if the brain tissue was not harvested shortly after the animal’s death, autolysis might make it very difficult to confirm a diagnosis by histopathology, but these tests permit a diagnosis of a TSE based on finding PrPres even if the brain has been frozen or if autolysis has occurred.

Last year, the European Commission published a preliminary report on the evaluation of four companies’ tests for the diagnosis of TSE in cattle brain samples. These included 1) immunohistochemistry testing of eyelid associated lymphoid tissue and tonsil biopsies, 2) use of capillary electrophoresis and fluorescent labeled peptides to detect PrPres in the blood of animals infected with a TSE, and 3) improved Western-blotting techniques with very good sensitivity to detect PrPres in blood, cerebrospinal fluid, or small pieces of biopsied tissues.

Agent Isolation: As the agents that cause TSE’s have not been fully characterized or isolated, one method used to detect infectivity in an animal is to inoculate laboratory animals with brain material from the affected animal and monitor them for evidence of disease. This method may take more than 2 years to produce results; hence, it is not practical for routine testing. The most common animal used for this type of bioassay is the mouse. Another problem with the mouse bioassay method when testing cattle or sheep samples is that the species barrier may prevent detection of low levels of infectivity.