

Bovine Spongiform Encephalopathy – Only a British Concern?

Mark M. Robinson *PhD*
Research Microbiologist
USDA-ARS Animal Disease Research Unit
Bustad 337, Washington State University
Pullman, WA 99164-7030

Introduction

Between November, 1986, and August, 1991, 35,100 clinical cases of bovine spongiform encephalopathy (BSE) were confirmed histopathologically by the staff of the Central Veterinary Laboratory (CVL) Ministry of Agriculture, Fisheries and Food in Weybridge, England. It is not known how many cases of BSE went unreported during this time period, but informal estimates range from several hundred to several thousand. These losses occurred within the prime production population of the United Kingdom's dairy and beef herds which number approximately four million adult animals (twelve million total cattle) in a geographic area approximately the size of Oregon. During the same period, novel spongiform encephalopathies were confirmed in nine zoo animals of various species, but all from the family bovidae. Also, spongiform encephalopathy was confirmed in nineteen domestic cats during the last sixteen months, and BSE was identified in native-born dairy cattle in Switzerland (7 cases confirmed) and France (4 cases confirmed) during the past ten months.

The advent of a novel, progressive, and transmissible spongiform encephalopathy in cattle and its rise to epidemic levels in the United Kingdom has caused substantial economic hardship for the dairy, beef, and rendering industries of that country. In addition, it has led to increased public concern about the quality of agricultural products in general and the effectiveness of the government agencies that regulate the production and consumption of those products. These concerns have been transmitted internationally such that a recurring question in Europe and the Americas is "Can BSE happen here?". A simple answer to this question is not available, but awareness on the part of U.S. bovine practitioners of the disease characteristics and the factors that contributed to the problem in the U.K. will help prevent a BSE-like epidemic from occurring in the United States.

The Transmissible Encephalopathies

BSE is the newest member of a small family of subacute transmissible spongiform encephalopathies that includes sheep scrapie, the chronic wasting diseases of mule deer and elk, transmissible mink encephalopathy (TME), and the human diseases kuru, Gerstmann-Straussler-

Scheinker syndrome (GSS), and Creutzfeldt-Jakob disease (CJD). The spongiform encephalopathies of cats and zoo animals in the U.K. are candidates for this group of diseases, but their transmissibility remains to be determined. Diseases in this group share the characteristics of i) incubation periods measured in months to years ii) a fatal outcome of the clinical disease, and iii) the appearance in nervous and lymphoid tissues of an abnormal form of a normal cellular protein which is referred to as PrP or prion protein. A primary difference between BSE and the other members of this group is that most of the transmissible encephalopathies have low annual incidences (e.g., CJD occurs in one out of every two million people per year worldwide) while BSE now affects four out of every one thousand cattle in the U.K. annually.

Clinical Signs

BSE was observed initially in Holstein and Holstein/Friesian dairy cows during 1986,¹ but has been documented in all of the dairy and beef breeds in the United Kingdom over the past five years.⁹ Clinical disease has been observed in cattle from 22 months to 15 years of age.⁹ The clinical signs have remained consistent over the course of the epidemic and may last from several weeks to months in an individual animal. The initial observation is usually apprehension, characterized by a reluctance to pass through doorways or into milking stalls. Tactile and auditory hyperesthesia, mild incoordination, kicking during handling, aggressive behavior towards other animals and handlers, and an appearance of fear usually follow. As the signs progress and become more pronounced, they may include loss of condition and weight, moaning, excessive salivation, pruritus, bruxism, and the development of exaggerated responses to auditory stimuli such that a loud or sharp noise may cause the animal to fall. Severe incoordination develops and also results in hypermetria and falling. If allowed to progress, the animal exhibits signs of frenzy, becomes totally unpredictable, and eventually will assume terminal recumbency. An ante-mortem diagnostic test is not available at this time, and supportive therapy is of minimal value. Euthanasia during the early clinical stage

is recommended.

Differential diagnoses include bovine rabies (not found in the United Kingdom), hypomagnesemia, central nervous system abscesses, neoplasias, or trauma, renal or hepatic encephalopathy, mineral or plant poisoning, and listeriosis. A definitive diagnosis is not always possible, but is dependent on the combination of a complete clinical history, appropriate ruleouts, and histological examination of suspect brain tissue. In cases where histological examination is inconclusive, an immunobiochemical test for the abnormal form of PrP can be made for confirmation of the disease.

Histopathology

Gross signs of spongiform change are generally not apparent when examining fresh BSE brain. Microscopically, discrete ovoid and spherical vacuoles are observed in the neuropil.¹ Intracytoplasmic vacuoles may be found in the dorsal nucleus of the vagus, the vestibular nuclei, and the red nucleus. However, these changes are not specific to BSE and may be observed in uninfected brain tissue, especially in aged animals. The important parameters for microscopic diagnosis are the locations and degree of vacuolation, not the finding that vacuolation is apparent.¹

A mild to severe gliosis may be apparent, particularly when special stains such as Cajal's gold sublimate are used. Also, intracytoplasmic aggregations of ceroid-lipofuscin pigment granules may be apparent in some vacuolated and unvacuolated areas.¹ Electron microscopic examination of biochemically treated brain tissue or tissue homogenates may reveal fibrils which are morphologically indistinguishable from scrapie-associated fibrils (SAF) of sheep and rodents.^{1,3}

History of BSE

BSE was first detected in late 1986 through microscopic examination of routine diagnostic submissions to the Central Veterinary Laboratory (CVL) diagnostic and research center in Weybridge, England. The initial cases described by Wells *et al.*¹ were in Friesian/Holstein cattle between three and six years of age. Since then, the disease has been documented in cattle between 22 months and 15 years of age.⁹ There is no breed predisposition for the occurrence of clinical BSE.¹⁰

Transmission studies using BSE-infected brain material in a variety of species have been carried out at several locations in the U.K. with results including successful transmission by intracerebral injection and oral dosing to mice,^{2,8} and parenteral administration to cattle,⁵ a pig,⁶ and sheep and goats.⁷

During 1987, epidemiologists at the CVL began a study to determine the most likely source of the BSE infection. Initial analyses indicated that the disease was typical of those originating from an extended common source and

that all affected animals were index cases.⁴ Retrospective analysis suggested that the first cases appeared during 1985. A survey of several hundred herds eliminated the possibility of a genetic cause for the disease and revealed no correlation between BSE and the importation of live animals, the use of semen, therapeutic agents or agricultural chemicals, or the association of BSE-affected animals with sheep or other animals.⁴ The most probable cause was identified as the feeding of sheep scrapie-infected meat and bone meal to cattle, beginning in approximately 1981.⁴ It was hypothesized that an increase in the incidence of sheep scrapie coincided with changes in rendering techniques, resulting in increased exposure of many cattle to scrapie-infected rations during 1981-1982.

More recent studies have demonstrated a strong regional correlation between the incidence of BSE, the elimination of hydrocarbon extraction from the rendering process, and the reprocessing of partially rendered offals (greaves).⁹ The use of hydrocarbon solvents for fat extraction has been eliminated from most rendering operations for environmental and safety considerations, but the two major plants in Scotland still use the solvents, and the incidence of BSE in that area is much lower than elsewhere. Likewise, the percentage of greaves in the starting material for any rendering plant is inversely proportional to the BSE incidence in the region, with more greaves being used in the northern U.K. where there is less BSE. While these correlations do not prove that BSE was caused by feeding scrapie-infected rations to cattle, they do show that feedstuffs are the most obvious route of introduction of BSE to the cattle population.

The incidence of BSE has increased steadily from 1986 to the present. Initially, only a few cases were detected monthly. When BSE was made a reportable disease in June of 1988, the number of notified cases increased, but still averaged between 100-150 per month. By the spring of 1989, the average was 200-250 cases per month. In the fall it was 500-600, and by the first of 1990 the average was approximately 1200 per month. In the fall of 1990, the notification rate averaged 1400-1500 cases per month, and at the present, the rate is over 2,000 per month.

Regulatory Measures in the United Kingdom

The government's response to BSE was fairly conservative due to previous experience with scrapie in the U.K. Initially, BSE was not judged to be a significant problem relative to salmonellosis and similar diseases. When it became clear that the incidence of BSE was increasing significantly, the Ministry of Agriculture (MAFF) made the disease reportable (June, 1988) and issued a ban on the feeding of ruminant derived protein supplements to ruminants (July, 1988). In August of 1988, the slaughter and incineration of BSE cattle was made compulsory. As of November, 1989, a ban on the human consumption of specific bovine offals (brain, spinal cord, thymus, spleen, ton-

sils, and intestines) was imposed. In September, 1990, the specified offals ban was extended to all pet and farm animal food as a result of experimental BSE transmission to a pig.⁶

Regulatory Measures in the United States

The BSE epidemic in the United Kingdom has been monitored closely by regulatory officials (APHIS) and research representatives (ARS) of the USDA since 1987. A total ban on the importation of live cattle and bovine products from the U.K. has been in place for three years. In addition, APHIS has conducted a survey to determine the location and disposition of all cattle imported from the U.K. during the 1980's. No evidence has been found that any of these animals had or have BSE.

APHIS, FSIS, and the CDC have surveillance programs in place through which the brains of cattle that succumb to non-specific central nervous system disorders are examined for microscopic indications of a BSE-like disease. Also, APHIS has subjected federal, state, and academic veterinarians to an intense educational campaign so that the appearance of a scrapie-like disease in cattle in this country will be more readily recognized.

On a broader scale, APHIS has placed renewed emphasis on the establishment of an effective scrapie control program by conducting negotiated rule making efforts that involved sheep industry representatives, research scientists, and related industry representatives such as meat packers and renderers. Informal efforts have been made to determine the necessity of regulations concerning the disposal of sheep through rendering and the use of ruminant-derived rendered products in animal feedstuffs. Voluntary actions initiated by the National Rendering Association have reduced the need for governmental action on these subjects at the present time.

Current Research Efforts

The number and scope of research efforts concerning scrapie-like diseases has increased dramatically since the advent of BSE and can only be summarized here. In the United Kingdom, a variety of studies have been initiated to determine 1) the transmissibility of BSE to other species, 2) the pathogenesis of BSE, 3) the causative agent of the disease, 4) if BSE is transmitted either vertically or horizontally, 5) if BSE infection can be avoided through embryo transplantation, and 6) if the BSE agent can be eliminated from domestic animal offals through improved

rendering practices. In addition, scrapie-related studies aimed at the development of an antemortem diagnostic test and the detection of genetically "resistant" animals have been augmented. Also, since the transmission of BSE to humans is a subject of major concern, a study is in place to monitor the incidence of human dementias over the coming decades.

In the U.S., the USDA Agricultural Research Service, National Institutes of Health, and independent academic laboratories are working to characterize the agents of BSE and scrapie and develop antemortem diagnostic tests for these diseases. A collaborative effort between ARS, APHIS, and several industries has resulted in a unique effort to test the hypothesis that sheep scrapie-infected meat and bone meal can cause disease in cattle. Results from this study should be available within the next several years.

Conclusion

The course of the BSE epidemic in the United Kingdom may not be known for several more years. Optimists predict that the incidence of BSE will peak during 1991-1992, while others prefer not to make predictions about an unconventional infectious disease that was unknown before 1986. BSE has not been detected in the United States and hopefully will never occur here. However, the history and characteristics of BSE bear thorough analysis whether the epidemic increases or disappears. This is because the BSE epidemic appears to have been induced through human manipulation of the food chain, which means that increased manipulation of the food chain, as is happening every day, may lead to similar or novel problems in animal health. Therefore, it is incumbent upon all animal health practitioners, particularly those involved with production medicine, to remain alert to the possible emergence of new diseases and help prevent the spread of these diseases within the livestock industries.

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