BOVINE SPONGIFORM ENCEPHALOPATHY (BSE):
The Current Situation and Research

R. BRADLEY
Pathology Department Central Veterinary Laboratory New Haw Weybridge Surrey KT15 3NB.

Key words: Bovine spongiform encephalopathy - Sub-acute transmissible spongiform encephalopathy - Prion disease - Slow virus disease - Neuropathology - Clinical signs - Epidemiology - Transmission studies - Molecular genetics - Molecular biology - Embryo transfer - Disease control - European Community Action

Bovine spongiform encephalopathy (BSE), discovered in Great Britain in 1986, was to pose one of the most serious threats to the well-being of the British cattle industry this century. The disease is now established as a member of the group of diseases known as the sub-acute spongiform encephalopathies caused by unconventional, transmissible agents and which includes scrapie of sheep. It is from scrapie of sheep that it appears BSE has resulted though it is possible BSE may have existed in a sub-clinical form in cattle. The vehicle of transmission is meat and bone meal prepared from infected ruminant carcasses and included in the protein concentrate rations of cattle, especially dairy cattle in which the disease predominates. Most animals become exposed as calves and the incubation period is typically 4-5 years with most cases occurring at this age. The increase in exposure of cattle to infection that resulted in disease in 1985/1986 was 1981/1982. The factors that contributed to this increase were an increasing sheep population, possibly an increase in the prevalence of scrapie and changes in the industrial processing of animal waste to prepare meat and bone meal. The clinical signs of BSE include abnormal behaviour, posture, gait and an increased sensitivity to visual and aural stimuli. There is loss of condition and milk yield. In only one of 28,197 cases of BSE confirmed by 10 May 1991 can feed be almost certainly ruled out as a source of infection. This therefore may be a singleton case of maternal transmission though we cannot be certain. Every other case so far has been exposed to meat and bone meal in the diet and thus resulted in an extended common source epidemic. A large research programme is underway to investigate the epidemiology, clinicopathology, transmission and molecular biological/genetic aspects of the disease. Much is collaborative between Institutes and Member States of the European Community, in which the disease, as in Britain, is notifiable. In Britain the lynch pin of control for animal health has been the ban established in July 1988 on feeling of ruminant protein to ruminant animals. Though there is no evidence that either BSE or scrapie is a hazard to humans, as a precautionary measure, suspect animals are compulsorily slaughtered and destroyed (except all brains are taken for diagnosis) with compensation being paid at 100% of value. Milk from such animals is also destroyed. The offals from all cattle over 6 months old likely to contain the agent of BSE are not permitted to be fed to any animal, poultry or bird. As a result of these measures the epidemic in Britain is expected to decline from 1992/1993 onwards and be extinct by the end of the century provided no cattle to cattle transmission occurs and for which at present there is no evidence.

INTRODUCTION

In November 1986 a discovery was made that was to pose one of the most serious threats to the well-being of the British cattle industry this century.
Pathologists at the Ministry of Agriculture, Fisheries and Food, Central Veterinary Laboratory at Weybridge had, as a result of the animal health surveillance activities of the State Veterinary Service, identified a scrapie-like disease of cattle, a condition which previously in food animals had been confined to sheep and goats. The new disease was named bovine spongiform encephalopathy (BSE) (46). Retrospective study of herd records suggested that the earliest clinical cases of BSE occurred in April 1985 although unrecognised at the time.

All suspect cases of BSE reported to the Ministry which have been slaughtered or have died have been examined clinically and by brain histology first voluntarily and since June 1988, when the disease was made notifiable, compulsorily. At 10 May 1991 there have been 28,197 confirmed cases on 11,746 farms only 1360 of which are occupied by beef suckler herds. At the same date 22,219 (91.0 per cent of all dairy herd results in no detectable immunological response even the latest member of the group of diseases known as the progressive, fatal, neurological disorder embracing vacuolation was scrapie-like was supported by the within dairy herds in Great Britain.

Confirmation that BSE is a sub-acute spongiform encephalopathy (SSE).

Conclusive evidence that BSE was a new member of the SSE group of diseases demanded two more vital pieces of information. First, that detergent-treated brain extracts treated with protease K and examined by negative stain electron microscopy (31, 32) showed the presence of 4 - 6mm diameter helically wound filaments named scrapie-associated fibrils (SAF). Such fibrils were found by Weybridge workers in specific areas of the brains of BSE affected cattle but not in the brains of clinically normal cattle without spongiform encephalopathy (41, 46). Workers at Weybridge, the Institute for Animal Health (IAH) Neuropathogenesis Unit (NPU) in Edinburgh and University of Heidelberg subsequently showed that the major protein of the BSE brain fibrils was the bovine homologue of the SAF protein (Protease-resistant protein, Prion protein or PrP) as judged by its size, protease resistance, immunoreactivity, lectin binding and partial N terminal sequence (21).

The second requirement was to demonstrate that BSE was a transmissible disease. This was first accomplished at NPU by the combined intracerebral and intraperitoneal inoculation of special laboratory strains of in-bred mice with homogenates prepared from the brains of four terminally-affected cattle from widely geographically separate areas of Britain. This resulted in the production of scrapie-like clinical signs (from 292 days post inoculation) and neuropathology similar to that seen in mice affected with scrapie from some primary sheep sources (15). This important work opened up many avenues for studying BSE. These included the use of the mouse for the biological assay of BSE infectivity in cattle tissues and products, for investigating the possible occurrence and features of agent strains, for determining the susceptibility to chemical and physical treatments and for identifying sources of infection. Thus it is now established that BSE is a confirmed member of the SSE group of diseases (Table 1).

Clinical signs

The progressive clinical signs of BSE were recorded from the onset of the epidemic both on farm and in selected cases after transportation to Weybridge where sequential neurological studies were undertaken in some cases for several months. Some cases ran short clinical courses of under two weeks whilst others extended to over one year. The introduction of compulsory notification and slaughter means that most cases are now killed soon after clinical disease is first suspected. The main clinical signs include apprehension, hyperaesthesia, abnormal behaviour, abnormal posture and gait ataxia. Loss of milk yield and bodily condition are usually evident a few weeks after clinical onset but sometimes may be included as part of the initial presenting signs. Many of the abnormal behavioural signs are exaggerated or abnormally persistent patterns of normal behaviour, such as repeated nostril or flank licking. Excessive salivation is not a feature of BSE and few cases run the normally short (< 8 days) clinical course of rabies which otherwise might be a differential diagnosis. Rubbing of head, tail and hindquarters, providing evidence of pruritis occurs but is not as consistent a sign as in sheep scrapie. Muscular tremors are frequently observed. In the natural disease no distinct pattern of variation in signs occurs between breeds. Some animals teeth grind, others emit constant moaning for variable periods. Bradycardia (mean 59 beats/min) was recorded in all of 14 cows examined in one study (49).

Electro-encephalography has been employed in a small number of cattle with BSE and has revealed significant differences in the traces obtained from these animals and similarly aged clinically normal cattle and from experimental neurological disease in other ruminants (44). However, under farm conditions and with present knowledge the technique is not considered practical for routine use.