

## **Bovine Spongiform Encephalopathy Summary**

### **Introduction**

1. This note provides a brief summary of an analysis undertaken by a DISCONTTOOLS group of experts on Bovine Spongiform Encephalopathy (BSE). They reviewed the current knowledge on the disease, considered the existing disease control tools, identified current gaps in the availability and quality of the control tools and finally determined the research necessary to develop new or improved tools. Full details of the analysis can be downloaded from the web site at <http://www.discontools.eu/> by selecting Disease Database, then the specific disease and highlighting the variables of interest. This is completed by selecting “create a report” which can then be downloaded as either a PDF or Excel spread sheet.

### **Disease profile**

2. The first cases of BSE were recognised in the UK 1986 as a neurological disease of adult cattle. BSE is a degenerative disease of the brain. Cattle are the main species affected although people have been infected as well as captive wild ungulates, goats and felines. Where the disease has occurred in other countries, it tends to have the same phenotype as the disease in the UK cattle population, and can usually be linked to the UK (either by movement of cattle or cattle feedstuffs).

3. The BSE agent is considered to be a prion which is comprised largely of a self-replicating protease resistant protein known as PrP<sup>Sc</sup>. This is involved in the pathogenesis of the disease and is considered to be the main or only component of the prion. Studies on the lesion profile indicate uniform brain pathology, both in cattle and in mice, following experimental transmission, suggesting only a single strain of BSE agent was present during the epidemic.

4. Unusual or atypical forms of BSE have been identified in a number of countries based on the molecular characteristics of PrP<sup>Sc</sup> in Western blots. Two different molecular PrP<sup>Sc</sup> patterns have been described, the L-type with low molecular mass and the H-type with high molecular mass of the protease-resistant prion protein. These do not have the same pathology, including the pattern of lesion distribution and PrP<sup>Sc</sup> accumulation in the brain. In addition, animals do not display the same clinical signs as classical BSE (C-BSE). Laboratory transmission experiments suggest that the L-BSE agent has a zoonotic potential, which appears higher than that of the C-type BSE agent. Given the rarity of these cases, their occurrence predominantly in aged animals and their widespread geographical distribution (including in countries with no history of C-BSE) it is speculated that these cases may occur spontaneously.

### **Risk**

5. Variant Creutzfeldt-Jakob disease (vCJD), first reported in March 1996, affects younger human patients and is linked to exposure to BSE. C-type BSE as well as L-type BSE are transmissible to humanised transgenic mice and non-human primates. No equivalent data exists for H-type BSE to date. There is no substantial information on the zoonotic potential of atypical forms of BSE, or sufficient epidemiological data with which to undertake any effective risk assessment.

6. Most cases of vCJD are believed to be of dietary origin, following ingestion of food containing the infective agent, particularly before the removal of specified bovine risk materials from food- and feed chains. Provided infected material is prevented from entering the animal feed chain BSE case numbers should continue to decline. However, the initial source of contamination was never identified. H- and L-type BSE are hypothesised to be rare spontaneous diseases, although many of the cases identified so far were born before the implementation of fully effective feed bans in the respective countries. It is possible that C-type BSE, like H- and L-types are hypothesised to be, is a rare spontaneous disease which could once again be amplified through feed if the ban on intra-species recycling of meat and bone meal is relaxed. Cases of all three types of BSE have been born after the most rigorous feed bans, but the numbers of animals are too small to make any robust epidemiological assessment of this.

7. The current strains of BSE do not spread between cattle as, for example, scrapie does in sheep, or CWD in cervids. If new types of BSE should appear which have the pathogenic and transmission characteristics of scrapie then control would be considerably more difficult and with the potential for higher risks to humans.

### **Diagnostics**

8. Commercial kits are available to confirm disease on examination of the brain material removed from an animal. These include high-throughput Western blot, lateral flow immunoassays and ELISA tests to screen large numbers of samples. There are limited opportunities for new developments in disease detection. There are sufficient tests available for the post mortem detection of PrP<sup>Sc</sup>. No alternative specific marker has been identified to improve any aspect of disease identification or confirmation.

9. The obvious gap is the lack of a diagnostic test to identify BSE in live animals. This would identify animals in the pre-clinical phase of disease, and could be applied to the screening of apparently healthy populations such as whole herds or specific animals for import or export purposes. The current problem with the development of tests is the availability of pathogenic material and animals incubating the disease. This makes the development and validation of tests very time consuming and dependent on others providing the material for the laboratory and field validation. From development through validation to commercial availability would take years.

Another important gap is in the absence of a test for the detection of environmental and/or feed contamination

### **Vaccines**

10. The development of vaccines so far pose an insurmountable challenge. In the event of vaccines being required, the time from development to approval will be lengthy as the pathogenesis is not fully understood and there is currently no evidence of an immune response. Very expensive and detailed research would be needed to unravel the pathogenesis and to identify whether a vaccine is feasible.

### **Pharmaceuticals**

11. Pharmaceuticals are not required for animal health applications. While some therapeutic potential would be highly desirable in the human field, the number of cases likely to occur is too low to drive this as a commercial interest.

### **Knowledge**

12. Multiple areas of uncertainty in the understanding and knowledge of BSE remain, especially in relation to pathogenesis, immunology and epidemiology. Early pathogenesis at both the animal and cellular level is still poorly understood, not least because of the lack of a good experimental model. No measurable humoral immune responses have been detected in BSE cases, and although the glial response in the brain constitutes a form of immune response, it is not one that results in a measurable diagnostic parameter. Various immunochemical tests have been developed for surveillance purposes using PrP specific antibodies, but these can only be applied post mortem. There is no immunological basis for diagnosis in the live animal.

13. There is still no satisfactory conclusion regarding the origin of the BSE epidemic. If C-type-BSE is, like H- and L-type are thought to be, a rare spontaneous disease, then relaxation of the ban on intra-species recycling of meat and bone meal could ultimately result in a repeat of the epidemic.

14. Research is needed to fill these knowledge gaps; many of these are closely linked to the requirements to develop more effective tools for the control of the disease. Full details of the gaps are shown in the Disease and Product Analysis for BSE on the DISCONTTOOLS web site.

**Conclusions**

15. The case numbers of C-type BSE have declined rapidly, which is undoubtedly related to the strict controls on ruminant protein and its use in animal feed. Occasional cases still occur (including recently in animals 5-8 year old, both in the EU and North America), many years after the feed bans were put in place. It is unclear whether these can be attributed to poor implementation or policing of the feed bans, or whether they support the hypothesis that, like the atypical types of disease, C-type BSE was originally a rare, potentially spontaneous disease of cattle, in which case occasional cases will continue to occur. In light of recent experimental findings it cannot be excluded that atypical BSE might have been the origin of C-type BSE. This highlights the fact that the origin of BSE has never been conclusively identified. All of this will have implications once existing bans and levels of surveillance are both relaxed.