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# Bovine spongiform encephalopathy Update

**Ray Bradley**

Veterinary Laboratories Agency, New Haw, Addlestone, KT15 3NB, United Kingdom, Email: raybradley@btinternet.com

**Abstract.** Bovine spongiform encephalopathy (BSE) is a zoonosis being the origin of variant Creutzfeldt-Jakob disease and an important cattle disease in its own right. Countries have been slow to learn the importance of protecting, not only their cattle populations, but also their human populations. Since 2000, several additional European countries have reported BSE in native-born stock and this has led to a concern about the BSE status of countries that have imported cattle and cattle products from infected countries. Extensive feed and offal bans and application of newly-developed, 'Rapid' tests for prion protein in central nervous tissue of targeted, high-risk animals and slaughter cattle over 30 months old now provides the tools whereby the public are fully protected and BSE can be eradicated.

**Key words:** BSE, amd cow disease, prion diseases

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## INTRODUCTION

The purpose of this article is to provide an update to 1 June 2001 of Bovine Spongiform Encephalopathy (BSE) in cattle and related new diseases of domestic cats and captive wild animals. This will include the geographical distribution of BSE in the world and recently introduced measures in the Member States of the European Union.

The distribution of BSE infectivity in the tissues of cattle naturally affected with BSE and during the incubation period of experimental BSE are important data on which to base measures. The results of research into the pathogenesis of BSE, concludes the report. Unless otherwise specified, the source of numerical data is the Department for the Environment, Food and Rural Resources (DEFRA), formerly the Ministry of Agriculture, Fisheries and Food (MAFF), *via* their biennial Progress Reports, BSE Enforcement Bulletins and other announcements.

## BSE IN CATTLE IN THE UK

BSE was first reported in 1987 (Wells et al. 1987) though the first confirmed case was in November 1986 and the probable first clinical case was in April 1985. By the end of 1987, the vehicle of transmission (meat-and-bone-meal or MBM) had been identified as a result of epidemiological investigation (Wilesmith et al. 1988). In July 1988 a ban on the feeding of ruminant protein to ruminant animals was introduced that should have completely prevented new exposures from feed. The ban was a vital concept in the attack on BSE and was effective but not completely so. This is clear from Fig. 1 that shows a marked and continuous decline in cases from 1993. The delay between the introduction of the feed ban and clear evidence of the decline is due to the long incubation period, which on average is 60 months, with a range from about 20 months to perhaps lifetime. That the ban was incompletely effective is confirmed by the fact that 42,299 cases of BSE (out of the total of 187, 870) have been confirmed in animals that were born after the 1988 ban was introduced; so-called born after the ban, or BAB cases.

A second ban, the specified bovine offals (SBO) ban was originally introduced in 1989 to protect the public from exposure to presumed infected tissues, had the host animal been exposed to BSE *via* feed. It was extended in 1990 to protect all species of mammal and bird after the successful experimental transmission of BSE to a pig following multiple parenteral routes of challenge with brain material from clinically affected cattle. The SBO comprised the brain, spinal cord, tonsil, thymus, spleen and intestine, from duodenum to rectum inclusive. The list was drawn up in ignorance of the real infectivity in these tissues but with the definitive knowledge that these tissues in natural scrapie of goats and Suffolk sheep were likely to be infected (Hadlow et al. 1980, 1982). The SBO ban itself was not completely effective in preventing processed animal protein from these offals getting back into the feed for animals. It therefore had to be strengthened. This was done in stages, first by specifying the skull rather than the brain, then by specifying the head rather than skull. Finally the head, spinal cord and spleen of sheep were added to what was now known as the specified risk materials (SRM) ban, because of the fear that BSE might have been transmitted to those sheep that consumed infected MBM. Finally, in 1996,

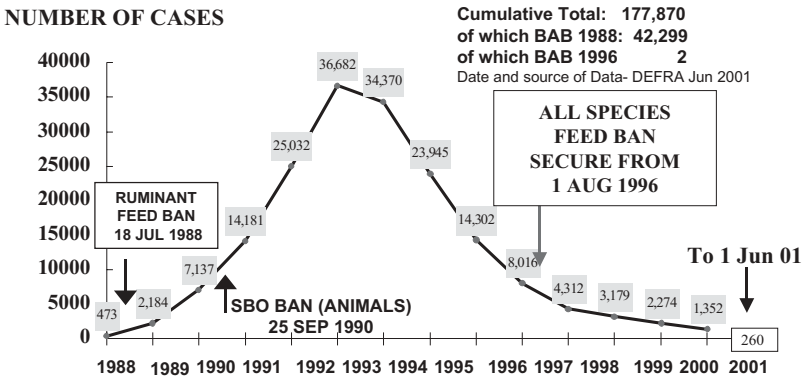



Fig. 1. The number of confirmed cases of BSE by year in Great Britain (Crown copyright).

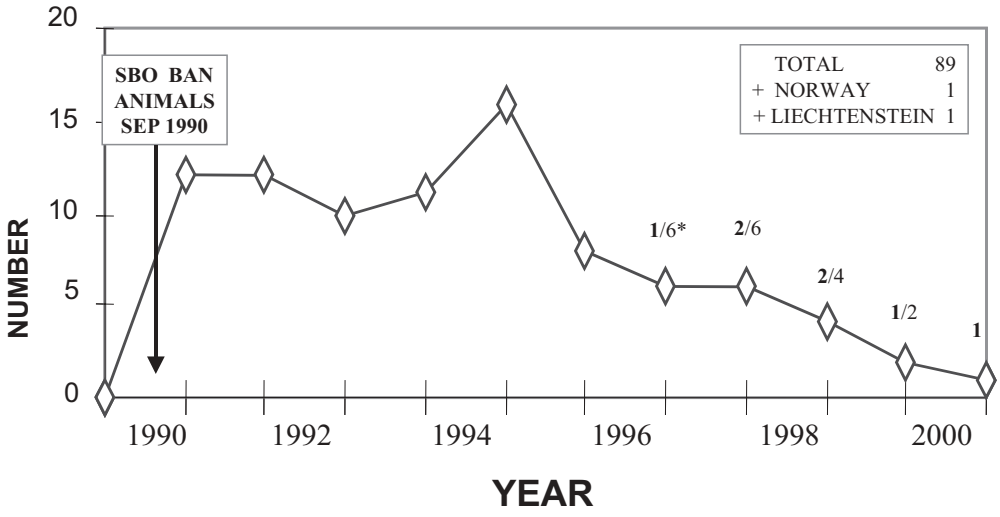
when the first ten cases of variant Creutztfeldt-Jakob disease (vCJD) were reported in the UK (Will et al. 1996) the Spongiform Encephalopathy Advisory Committee advised that mammalian MBM should no longer be fed to any food animal species including horses and fish. This became law in April 1996 and was deemed to be effective from 1 August 1996 when all feed containing MBM had been withdrawn and destroyed. Notwithstanding this draconian action, two cases of BSE were identified by June 2001 that had been born after this ban.

Early epidemiological studies revealed that dairy cattle were most affected by BSE and this was attributed to the way these animals were fed in early life. Calves from dairy cows are removed from their dam usually within 24 hours of birth and fed initially on artificial milk. They are soon weaned on to a diet of good quality hay and a calf starter ration. Until July 1988 the starter ration might have contained ruminant-derived MBM. Calves derived from the beef suckler herd, on the other hand, are suckled by the dam and supplementary concentrate feed is not normally required or given. The confirmed incidence of BSE in dairy herds to June 2001 is 61.3% and in beef suckler herds only 16.6%, indicating that the original explanations continue to apply. The total herd incidence is 37.5% which means that in the UK, even to-day, 62.5% of herds have been unaffected by BSE. The youngest case recorded was in a 20 month old cow and the oldest 19 years 9 months. Cases in such old animals might have occurred as a result of adult exposure.

## FELINE SPONGIFORM ENCEPHALOPATHY (FSE) IN DOMESTIC CATS

FSE was first reported by Wyatt et al. (1990) in a five years old neutered Siamese cat in England, presenting with a history of progressive fore- and hind-limb ataxia over a period of six weeks. There was no response to treatment and euthanasia was performed. *Post mortem* examination revealed no gross findings. Microscopic examination of the brain showed grey matter neuropil spongiosis, vacuolation of neuronal perikarya and astrocystosis, the cardinal features of a scrapie-like spongiform encephalopathy. Subsequently, further reports of similar cases were found in Great Britain and Northern Ireland (total 89 cases to June 2001), with one case each being reported in Norway and Liechtenstein. Transmission studies in mice using brain material from three cats showed that the disease is transmissible. Furthermore, the biological strain type of the agent isolated from the cats is indistinguishable from that isolated in the same inbred mice strains following challenge with the BSE agent from brains of cattle with BSE (Bruce et al. 1994).

The immediate protection of domestic cats from exposure to the BSE agent, that is believed to have resulted from oral ingestion of infected feed, was achieved by the 1990 SBO ban. This, although initially incomplete, appears now to be effective in eliminating new exposures of cats to BSE *via* feed. The annual incidence of FSE is shown in Fig. 2.




* Figure in **bold** type indicates the number born after the 1990 SBO ban

Fig. 2. FSE in domestic cats: incidence by year of report (Crown copyright, DEFRA Jun 2001).

## TSE IN CAPTIVE WILD ANIMALS

TSE almost certainly related to BSE (but as yet not proven by experimental challenge) has been reported in five species of captive wild Felidae in Great Britain (GB) (Bradley 1997). These are: cheetah 5 cases (with five further cases in cheetah exported from the UK to Ireland (1), Australia (1) and France (2+1unknown)), lions 3, ocelots 3, pumas 3 and tigers 3. All of these are assumed to have been exposed following consumption of uncooked cattle carcasses containing infected central nervous tissue. This might have been present in heads, necks or other parts of the vertebral column. Protection was secured by the 1990 SBO ban and there have been very few cases that were born thereafter.

TSE has also been reported in captive wild Bovidae in GB (Bradley 1997), but not elsewhere or in any natural environment inhabited by these animals. Eight species have been affected. In two, a nyala and a greater kudu, brain tissue has been inoculated into in-bred strains of mice. This shows the disease is experimentally transmissible and that the agent responsible is biologically indistinguishable from the BSE agent, *i.e.* it is of the same strain type (Bruce et al. 1994). The number of confirmed TSE by species is: Arabian oryx, bison, gemsbok, nyala and scimitar-horned oryx, one each; ankole, two; eland and greater kudu, six. All these species have presumably been exposed to infected MBM in concentrate diets that had similar formulations to those used in cattle feed before 1988. The reason for the cases occurring after 1988 (BAB cases) is, as in cattle, presumably cross contamination of diets with MBM intended for use in non-ruminant species. So far as records permit, no cases have been reported in animals born after January 1993.

## BSE IN CATTLE OUTSIDE THE UK

BSE has been reported in cattle imported from the UK in Canada (one case) the Falkland Islands (one case) and the Sultanate of Oman (two cases). Each has been identified, accurately diagnosed and completely destroyed and so present no further risk.

Until June 2001, BSE has been restricted to Western Europe (Fig. 3). Tables I and II show the number of cases confirmed by country divided arbitrarily into the major and minor players. It should be remembered that absolute numbers should be related to the size of the cattle population in each country (Fig. 4). In this regard the incidence of BSE by country is a better measure of the

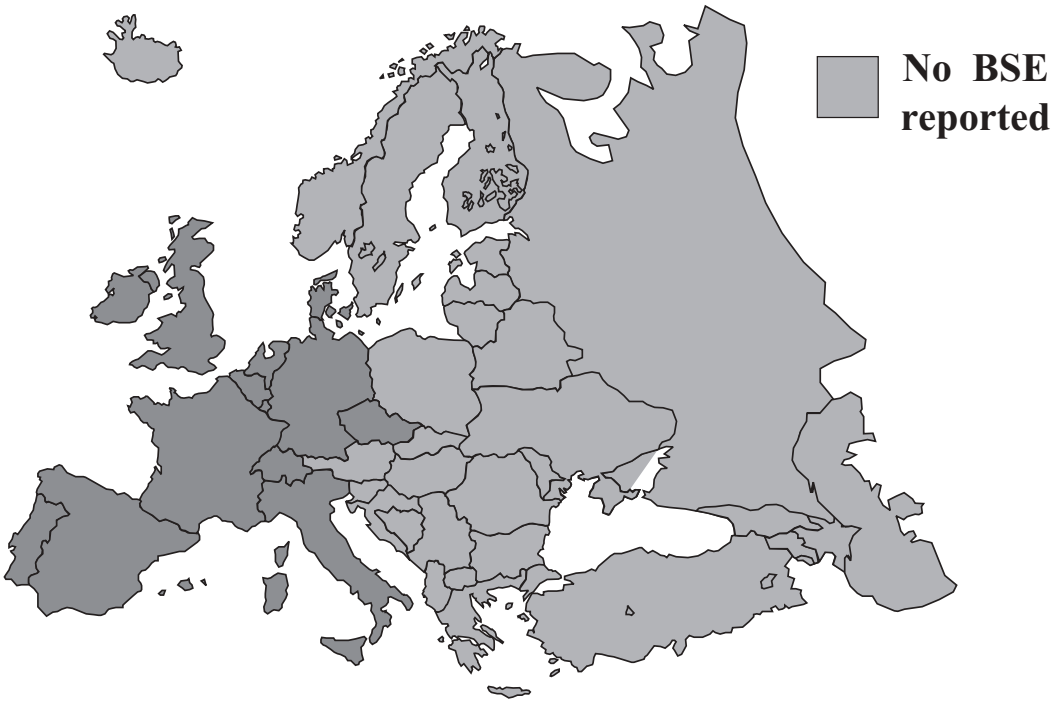



Fig. 3. BSE in Europe as at 1 June 2001 (Crown copyright).

severity of the BSE problem. The UK has by far the most cases and the highest incidence.

Originally, virtually all cases of BSE were identified by passive surveillance, *i.e.* reliance was placed on farmers, veterinarians and others in the livestock industry to report suspect cases to the competent authority. Latterly, starting in Switzerland, some countries have initiated active surveillance (Doherr et al. 1999, Schaller et al. 1999). Recently developed and evaluated "Rapid" tests for prion protein (Moynagh and Schimmel 1999) have been used on central nervous tissue of high risk and other cattle, such as fallen stock, emergency slaughter cattle and some adult cattle slaughtered for human consumption. In many cases BSE was subsequently confirmed by other statutory tests such as microscopic examination of the brain or conventional Western blotting. Some countries undertook such testing as part of a research programme. This procedure identified cases of BSE that had not been suspected and thus increased the confirmation rate. In Switzerland for example, 50% under reporting was detected. Subsequent to these successful national initiatives of targeted active surveillance, a EU-wide programme was introduced, partly to improve surveillance for BSE, but also, in the case of slaughter cattle over 30 months old, to improve consumer confidence in beef produced from them.

During the course of 2000 and into 2001, countries without reported cases of BSE in native-born cattle started to report them. These countries included Denmark, Germany, Italy, Spain and the Czech Republic.

Table I

Countries with BSE in native-born cattle - the major players

| | | | |
|---|---|---|---|
| GREAT BRITAIN[#] | 177,870 | | (47) |
| NORTHERN IRELAND[#] | 1,812 | | (76) |
| OTHER BRITISH ISLES[#] | 1,285 | | |
| FRANCE* | 302 | (1) | (96) |
| REPUBLIC OF IRELAND* | 627 | (12) | |
| PORTUGAL* | 574 | (7) | |
| SWITZERLAND* | 382 | (1) | (55) |
| OTHER COUNTRIES* | 190 | | |

( ) First column of which: No. imported; ( ) second column of which: No. found in a research or investigation programme. [#], data from DEFRA/DARD; *, data from OIE;

Table II

Countries with BSE in native-born cattle - the minor players

| | |
|---|---|
| BELGIUM | 34 |
| CZECH REPUBLIC | 1 |
| DENMARK | 2 (1 Imported) |
| GERMANY | 85 (6 Imported) |
| ITALY | 1 (2 Imported) |
| LUXEMBOURG | 1 |
| NETHERLANDS | 15 |
| SPAIN | 47 |
| LIECHTENSTEIN | 2 |

Some cases were reported as suspect cases and others were identified by use of "Rapid tests". These are included in Table II. These changes to the geographic distribution of BSE introduced additional problems in world trade. Countries without reported BSE in native-born animals in the 1990s had exported both live cattle and cattle products, including MBM, in the belief that no BSE existed within their boundaries. Countries receiving these exports were now themselves at risk from the occurrence of BSE, not only in the imported animals, but also within their native cattle population if infected feed in the form of MBM, or other infected ruminant protein products had been fed to them. The Scientific Steering Committee (SSC) of the European Commission (EC), as a result of a geographical risk assessment (see below), also anticipated such risks.

The epidemic of BSE is dynamic. A snapshot view of the current situation should pay regard to the dynamic dimension rather than just total cases (Fig. 5). In this regard it is important to determine if the epidemic is falling (as it is in the UK), if it is rising (as it is in the Republic of Ireland and France) or whether there is still some uncertainty as in Portugal and Switzerland. It is encouraging to note that the annual incidence does appear to be on the wane in the Portugal and Switzerland, and this may be confirmed by the end of 2001. In the latter country, the upward kink in the curve was against a background of low numbers of cases that were increased as a result of targeted active surveillance (Doherr et al. 1999). Active surveillance was also undertaken in cattle in the over thirty months scheme (OTMS) in the UK and in France as indicated in Fig. 5.

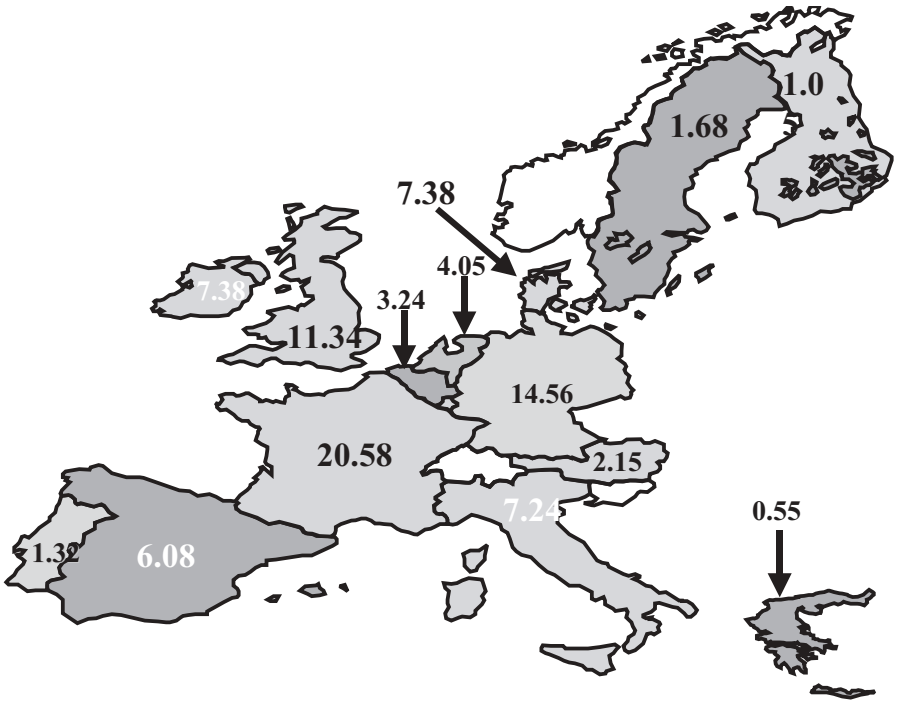



Fig. 4. Cattle populations in the EU in millions (Crown copyright).

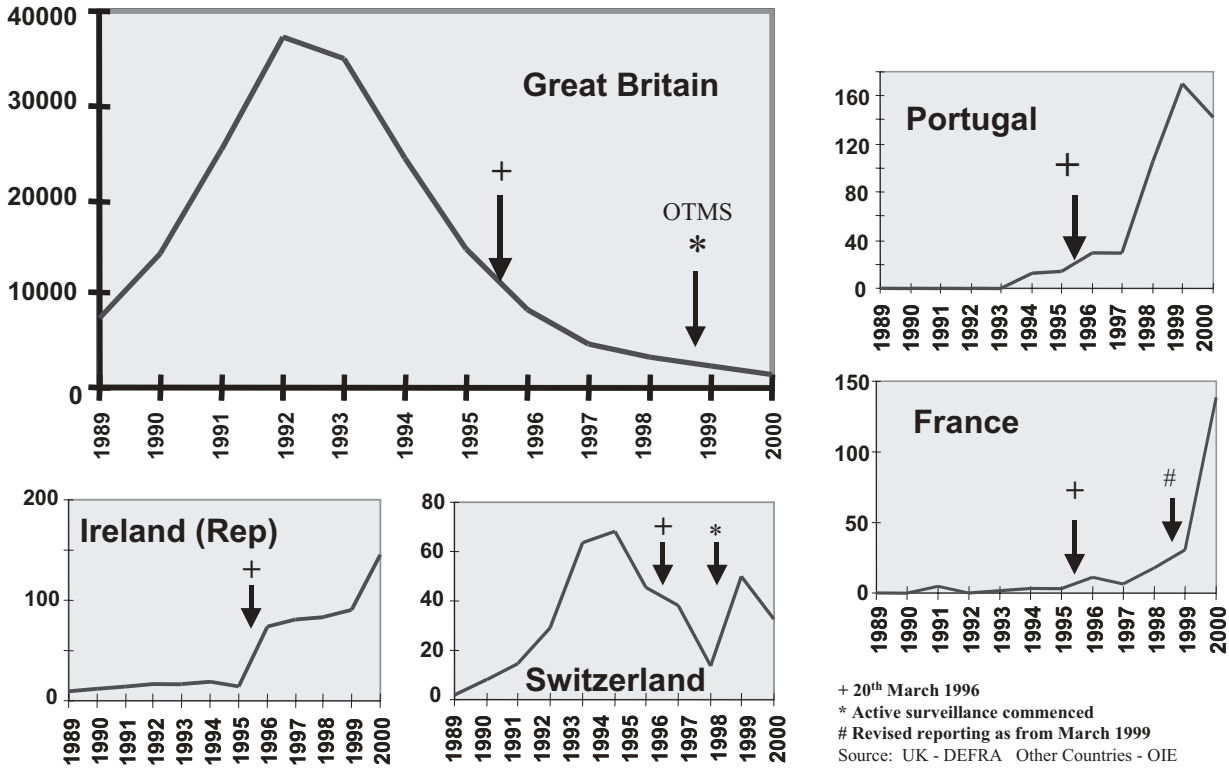



Fig. 5. Epidemic curves by country (Crown copyright).

## RECENT BSE CONTROLS IN THE EU

### Geographical BSE risk assessment (GBR)

The SSC has made an assessment of the BSE risk in Member States of the EU and third countries trading or wishing to trade with the EU in cattle and cattle products. This has been done by independent experts recruited for the purpose by close scrutiny of dossiers submitted by individual countries. The dossiers are compiled to include data and information requested by a Commission document prepared for the purpose. Countries have been classed into one of four categories dependent upon their assessed BSE risk taking account, for example, of the demography of their ruminant populations, the nature and enforcement of import controls, the ruminant and materials imported in the risk period, the methods of rendering animal waste and the method of feeding ruminant animals.

The Office International des Epizooties (OIE) in the International Health Code chapter on BSE has, for several years, set and modified the criteria for classifying countries. Currently (OIE 2001), countries are classified into one of five classes based principally on the incidence of reported BSE. However, the OIE has made no attempt to do other than lay down the recommendations for classification, so there are no OIE authorised lists of countries by category. It is intended that there should be an alignment between the OIE and EC criteria in the future. How the two sets of categories are currently related is shown in Table III.

The classification of countries by the EC SSC as at 1 June 2001 is shown in Table IV. Figure 6 shows the classification of European countries that have submitted dossiers and which so far have been analysed.

Table III

Relationship between OIE and EC BSE risk categories

| | EC | OIE |
|---|---|---|
| I | Highly unlikely | BSE-free |
| II | Unlikely but not excluded | Provisionally free<br>No indigenous case<br>Indigenous case(s) |
| III | Likely but not confirmed or confirmed at a lower level | Low incidence |
| IV | Confirmed at a high level | High incidence |

## RECENT OR PROPOSED EC REGULATIONS OF RELEVANCE TO THE CONTROL OF BSE

The European Parliament and Council have published a comprehensive Regulation (EC 2001 d) that lays down the rules for the control and elimination of certain TSE including BSE. This is effective from July 2001 but includes some transitional measures that shall be adopted for a maximum period of two years in order to permit the changeover from current arrangements to

Table IV

Geographical BSE risk (GBR) assessment by the EC SSC

| CATEGORY | |
|---|---|
| I | Argentina, Australia, Botswana, Brazil, Chile, Costa Rica, Namibia, Nicaragua, Norway, New Zealand, Paraguay, Singapore, Swaziland, Uruguay |
| II | Austria, Canada, Colombia, Finland, India, Mauritius, Pakistan, Sweden , USA |
| III | Albania, Belgium, Cyprus, Czech Republic, Denmark, Estonia, France, Germany, Ireland, Italy, Hungary, Lithuania, Luxembourg, Netherlands, Poland, Romania, Slovak Republic, Spain, Switzerland |
| IV | United Kingdom, Portugal |

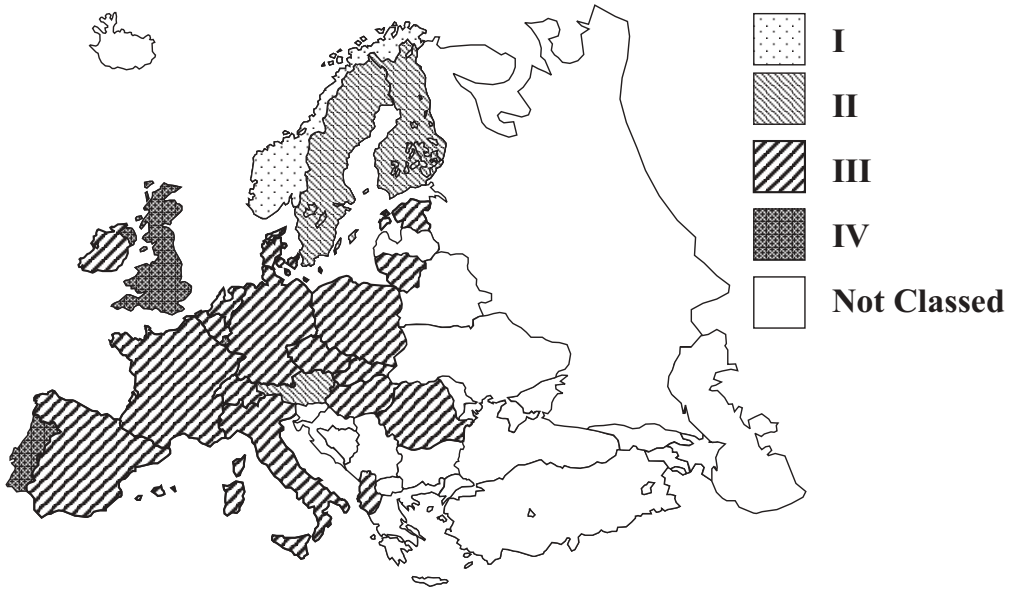



Fig. 6. EC SSC geographical BSE risk categories (Crown copyright)

the arrangements established in the Regulation. There is also a requirement to consult the appropriate scientific committee of the EC covering any question that could have an impact on public health.

A proposal for a Regulation of the European Parliament and of the Council laying down health rules concerning animal by-products not intended for human consumption has also been published and is expected to become law by early 2002. The key issue of this proposal is to prohibit the recycling of certain animal by-products into the feed chain, namely dead or condemned animals or their tissues. Furthermore, because TSE generally transmit more readily within species than between species and because within species recycling encourages the selection of pathogenic strains of agent, animal by-products will not be permitted to be fed to the same species from which they were derived. Furthermore, the only raw material allowed for use in animal feed would be that derived from animals declared fit for human consumption. Alternative methods for the disposal and traceability of animal products are introduced and links are established with Community environmental legislation. The proposal creates a new and simplified single legal framework to deal with the animal by-products sector not intended for human consumption.

### EC legislation on feed 2001

All European countries with BSE in their native-born cattle introduced some form of ruminant protein feed ban before, or soon after, the disease was detected in their country (e.g., UK, 1988, Denmark, France, Ireland Netherlands and Switzerland 1990). It was not until 1994 that there was common legislation for all Member States of the EU, which banned the feeding of mammalian MBM to ruminant animals. However, as indicated above, these bans whilst effective, were not completely so and all countries with BSE in native-born animals subsequently reported BAB cases of BSE. These are believed to be attributable largely, if not entirely, to cross contamination events as illustrated in Fig. 7.

To deal with this risk the EC introduced a temporary feed ban from 1 January 2001 (EC 2000 b). This prohibits the feeding of processed animal protein, with exceptions for milk and one or two other specific products, to all farmed animals kept, fattened or bred for food. In this context processed animal protein was defined to include: MBM, bone meal, blood meal, dried plasma and blood products, hydrolysed proteins, hoof meal, horn meal, poultry offal meal, feather meal, dry greaves, fish-meal, dicalcium phosphate, gelatine and similar products. The UK, which from 1 August 1996 had a mammalian MBM feed ban for all species, was required to extend it to align its legislation with that of all EU Member States.

### Stunning of cattle

From 1989 in the UK, when guidelines were being drafted (and subsequently adopted on an EU basis *via* the Committee on Proprietary Medicinal Products and

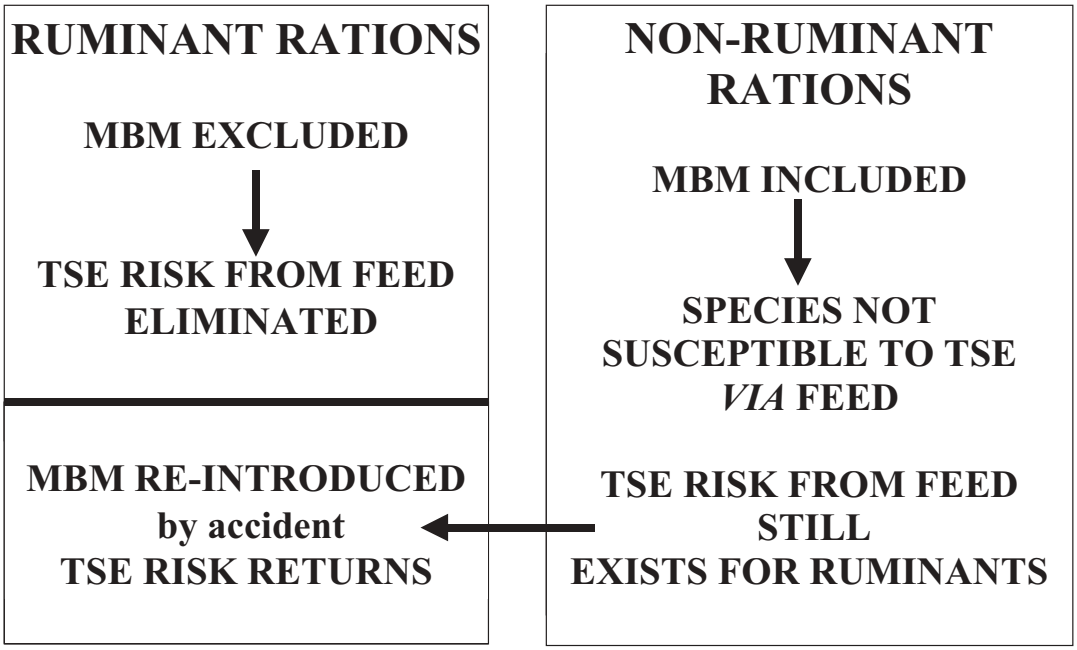



Fig. 7. The principle of cross-contamination events (Crown copyright).

Committee on Veterinary Medicinal Products) to reduce any risks in bovine starting materials used for the manufacture of biological and medicinal products, brain penetrative stunning of source animals was identified as a risk factor. This was because there was perceived to be a risk that brain material might be circulated as emboli to remote tissues as a result of the cerebral trauma induced by penetrative stunning. This supposition was subsequently converted to fact by studies in the US and in the UK that identified emboli, or evidence of embolic spread, following the use of a penetrative stun gun that injected air under pressure into the cranial cavity (Garland et al. 1996) or a conventional penetrating captive-bolt pistol operated with a cartridge and followed by pithing (Anil et al. 1999). Although the emboli could create a risk in an animal stunned by these methods if it was incubating BSE and infection was present in the brain (probably for at least 3 months before the onset of clinical signs (Wells et al. 1998), the majority of any dispersed infectivity would be in the venous blood draining the head, the heart and lungs. As cattle are killed by severing the major blood vessels at the entrance to the thoracic cavity immediately after stunning, at least some emboli might be present in the blood so collected. More studies are required to determine whether or not infectivity enters the arterial system of the systemic circulation, but the use of a penetrating captive bolt pistol alone (i.e., without pithing) does not result in the formation of brain emboli, (Anil et al. 1999). To manage the risk from emboli in ruminant species the risk methods of stunning were prohibited from 1 October 2000 (EC 2000 a).

**Rendering**

Following experimental studies using porcine abattoir waste spiked, either with brains from cattle with BSE, or from sheep with scrapie, a number of rendering processes were shown to be ineffective at inactivating the BSE and/or scrapie agent. Although no method of rendering can be guaranteed to inactivate all TSE infectivity, particularly if the starting titre is high, pressure-cooking of waste reduced to a particle size of 50 mm diameter or less, at 133°C, 3 bar, 20 minutes, is the most effective available and is the only method permitted for use for rendering mammalian waste. Other methods giving equivalent reductions in titre could be authorised after reference to the appropriate committee.

**Exclusion of raw (animal waste) material for feed use**

Clearly, reliance should not be placed on any rendering system to inactivate TSE agents completely, and therefore there is a need to exclude risk materials from the starting materials that might finally be converted to

MBM and tallow and included in animal feed. These exclusions, specified in a "Commission Decision EC 2001 b" include fallen stock, animals dying in transit, experimental animals, pet animals, zoo, wild and circus animals and animals killed for disease control purposes.

### Specified risk materials (SRM)

From the outset, several countries introduced national legislation to manage the risk of potentially infected bovine (and latterly ovine) tissues from clinically healthy animals getting into the human or animal feed chains. For example, in the UK in 1989 a specified bovine offals ban was introduced first for the protection of public health and in 1990 to protect animal health. Several other countries like Switzerland followed suit after BSE was discovered in that country. Although some other countries like France and Ireland adopted a restricted form of offals ban, it was not until October 2000 that a comprehensive EU-wide ban came into force and even this had to be extended in January 2001 (EC 2001 c) (Table V) to include the vertebral column (excluding the tail vertebrae). Derogations have been permitted for the UK in regard to removal of the vertebral column because the additional measures applied (such as only permitting cattle under 30 months old, or cattle under 42 months old from the Beef Assurance Scheme for human consumption) determine that any risk from this tissue in the UK is negligible. All other healthy cattle are destroyed within the Over Thirty Months Scheme (OTMS).

### Rapid PrP tests

Testing brain material for infectivity can only be done by bioassay. This is expensive and takes a minimum of a year to complete and often much longer. It is thus impractical for use in the abattoir situation.

There is a sound correlation between the presence of infectivity and the disease-specific form of the prion protein ($PrP^{Sc}$) in central nervous system (CNS) tissue which, when applied to CNS tissue of clinically suspect animals can be relied upon to act as a proxy for infectivity. Internationally agreed standard methods for the confirmation of BSE, namely by microscopic examination of the brain, detection of $PrP^{Sc}$ by Western blotting, immuno-histochemistry and detection of scrapie-associated fibrils by electron microscopy are listed in the OIE Manual, (OIE 2000). During the course of the BSE epidemic, more practical and rapid methods to detect PrP have been developed and evaluated. These are the so-called "Rapid" tests, (Moynagh and Schimmel 1999). Three rapid tests are now are determined to be reliable, practical and accurate, even though there is no published evidence that they reliably detect $PrP^{Sc}$ and by inference infectivity, in cattle incubating BSE. Nevertheless, they are now being applied in the field to detect BSE in high-risk populations as part of a

Table V

Specified risk materials in the EU

## ALL MEMBER STATES

| | |
|---|---|
| **Bovine, ovine & caprine animals over 12 months:**<br>**SKULL BRAIN EYES**<br>**TONSIL SPINAL CORD**<br>**VERTEBRAL COLUMN* + DRG (Excluding tail)** | **SPLEEN** |
| **Bovine animals of all ages:**<br>**INTESTINES (from duodenum to rectum)** | |

## ADDITIONALLY IN UK & PORTUGAL #

**Bovine animals over 6 months**

**HEAD (Excluding tongue) BRAINS EYES TRIGEMINAL GANGLIA**
**TONSILS THYMUS SPLEEN SPINAL CORD**

**(Commission Decision 2001/233/EC)**

* EXCEPT conditionally in the UK, Portugal, Finland, Austria and Sweden
\# EXCEPT the Autonomous Region of the Azores

surveillance programme in the EU. These high-risk populations include fallen stock, emergency slaughter animals and animals that show nervous signs when presented for slaughter for human consumption.

Furthermore, to improve consumer confidence in beef, from 1 January 2001, all slaughter cattle for human consumption over 30 months old and all emergency slaughter animals in the EU must pass an approved rapid test done in an approved laboratory, before the carcase can be passed for human consumption (EC 2001 a). In the case of a positive test, the carcase and organs of the particular animal, the one preceding it and two that follow it in the carcase line must be destroyed by incineration or exceptionally by burning or burial. Additional rapid tests are currently undergoing evaluation.

## PATHOGENESIS OF BSE

The pathogenesis of BSE and tissue distribution of infectivity at different ages is important to understand. To investigate this and to take account of the different tissue distribution of infectivity in cattle with BSE from that of sheep with scrapie (upon which information the original UK 1989 offals ban was based) an experimental study was undertaken (Wells et al. 1998). Thirty cattle were dosed orally with 100 g of brain material from confirmed BSE cases. There were ten un-dosed controls. At approximately four-month intervals and starting at six months of age (two months after dosing), three cases and one control were killed and over 40 separate tissues were collected aseptically for bioassay in mice by the intracerebral route. Because mice may under-estimate any infectivity present by around 500 times (Wells 2001) several important tissues are being bio-assayed in cattle by the intra-cerebral route thus eliminating the species barrier and maximising the sensitivity of the assay. To June 2001 no tissue that has shown no detectable infectivity after bioassay in mice, has shown detectable infectivity during bioassay in cattle by the intra-cerebral route, though none of these studies is yet complete.

The Pathogenesis study was undertaken to ensure that the selection of tissues classed as risk tissues in 1989 and previously based on scrapie data is reliable, and more importantly, to identify edible tissues that are uninfected throughout the incubation period and into the clinical phase of disease. The results of the mouse bioassay are summarised in Fig. 8.

As part of a study to show the comparative efficiency of bioassay in cattle and mice a pool of spleens and a pool of lymph nodes from five cattle with BSE have shown no detectable infectivity after challenge of either species by the intra-cerebral route (Wells 2001). This indicates that these tissues contain at least one million times less infectivity than brain does, from clinically affected cattle. In addition, challenge of mice by either the oral or the intra-cerebral route with milk, collected at early, middle and late lactation, from cows clinically affected with BSE, also show no detectable infectivity. Both in natural (MAFF 2000) and experimental BSE (Wells et al. 1998), it is clear that the distribution of infectivity during the incubation period and in the clinical stage of disease is much more restricted than it is in sheep (Hadlow et al. 1982) and goats (Hadlow et al. 1980) with natural scrapie. In cattle, infectivity is confined to the distal ileum during most, but not all of the incubation period and is present otherwise only in the central nervous tissue for a maximum period of just less than nine months and possibly for only three months before the onset of clinical signs (Fig. 8).

Table VI

Results from the use of "Rapid" PrP tests on high risk cattle

**TESTING OF ADDITIONAL BRAINS**

**(Confirmed by microscopic examination of the brain)***

**from fallen stock, emergency slaughter and OTMS cattle or detected as a result of active surveillance in a research (France) or investigation programme (Switzerland)**

| | 1998 | 1999 | 2000 | 2001 |
|---|---|---|---|---|
| **Switzerland** | **6*** | **22*** | **16*** | **11*** |
| **UK OTMS** > 5 years old | | **18*** | **39*** | **-** |
| **France** | **-** | **10** | **60** | **12 + 14$** |

$ = 14 cases detected by abattoir screening of cattle > 30 M old

## OUTSTANDING ISSUES

Expert groups of the EC SSC are currently evaluating any residual risks there may be in ruminant fat, tallow, gelatin or in the after the use of alternative rendering processes. Further GBR assessments are in progress and in addition, more "Rapid" tests are being evaluated. An important issue is to determine if there are alternative ways in which BSE can be transmitted to cattle than *via* infected feed (the major route) or possibly by maternal transmission (a possible minor route). In other words is

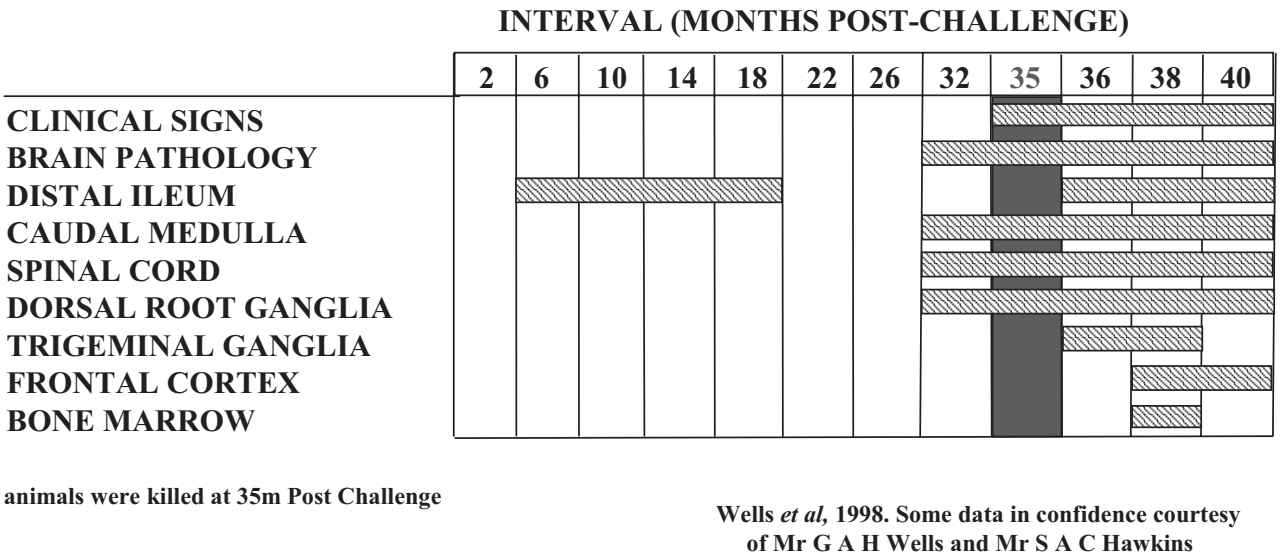



Fig. 8. Clinical signs, brain pathology and tissue infectivity by interval from challenge during the pathogenesis of experimental BSE in cattle following oral exposure to infected brain (Crown copyright).

there a "Third way" of transmission? The outcome of these studies and evaluations will be publicly reported as Scientific Opinions by the SSC when they are complete.

## CONCLUSIONS

BSE is declining towards extinction in the UK and probably also in Portugal and Switzerland. The epidemics in other countries will follow suit provided the current measures applicable in all Member States of the EU are strictly enforced. Although the incidence of BSE is still highest in the UK, beef and beef products are as safe as anywhere in the world because all the measures are strictly enforced, no mammalian MBM has been fed to any food animal species since 1 August 1996 and all cattle over 30 months old are excluded from the human and animal feed chain under the OTMS. A small number of forage-fed beef cattle up to 42 months old in the Beef Assurance Scheme are also permitted for human consumption but they, like all cattle over 30 months old in the EU must pass an approved "Rapid" test before this is permitted. This same test is also applied to targeted, high-risk animals in the EU and adds a new dimension of active surveillance to the already present passive surveillance scheme. Because since 2000 several additional European countries have reported BSE in native-born cattle, any country that has imported live cattle or products (other than milk or semen) may be at risk of introducing BSE. Risk analyses and surveillance for BSE as recommended in the OIE "Code" chapter on BSE are essential requirements to maintain security from this damaging disease. The use of "Rapid" PrP tests on targeted populations of adult cattle is an additional weapon in the armoury to establish the true status of animal health in regard to BSE and to detect the disease at an earlier stage than might otherwise be the case. Identification and complete destruction of clinically BSE-suspect animals and the removal of SRM are collectively the most important immediate measures to apply to ensure that public health is protected. In the longer term eradication of BSE from the world is the most secure way of protecting both public and animal health from this scourge. BSE has had a catastrophic effect on the livestock industry of Western Europe, and indeed the world. As a result of the application of the results of veterinary and other research the future now seems much brighter. Provided there is no relaxation on the current programme of research and its practical application the enemy will be defeated. This is an essential aim because any weakness in our defence can unfortunately have potential or actual repercussions upon human health, i.e., the occurrence of vCJD. This must be avoided at all costs.

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