Bovine Spongiform Encephalopathy

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Bovine spongiform encephalopathy (BSE) is a transmissible spongiform encephalopathy (TSE) described in Great Britain in 1987. The disease subsequently developed to an epizootic with greater than 180,000 cases occurring in Great Britain. There are a number of transmissible spongiform encephalopathies that infect animals and man but it must be emphasized that each has its own epidemiology, method of transmission and infectivity and the findings with one transmissible spongiform encephalopathy cannot be extrapolated to another. Much of our knowledge of BSE results from the occurrence and control of BSE in Great Britain.

Age incidence

Like all transmissible spongiform encephalopathies BSE has a long incubation period, 2.5 years at a minimum and possibly for the lifespan of cattle as the maximum. Epidemiological studies suggest that most affected cattle in Britain were infected as calves and the modal age at onset of clinical signs is between 5 and 6 years but there is a skewed distribution with the youngest age at onset recorded at 22 months and the oldest at 15 years. During the course of the outbreak there has been a change in the age distribution of cases in both Great Britain and Northern Ireland consistent with a sudden decrease in exposure as a result of the bans on ruminant protein feeding.

Clinical signs

The disease is insidious in onset and the clinical course progresses over several weeks varying from 1 to 6 months in duration but the case fatality is 100%. The disease has been given the name “mad cow disease” although this is a poor descriptor as frenzy is a minor clinical manifestation. There is a constellation of clinical signs with alterations in behaviour, temperament, posture, sensorial and movement. . Behavioural changes are gradual in onset and include changes such as a reluctance to pass through the milking shed, a change in milking order and a reluctance to pass through passageways. Affected cattle are disoriented and may stare, presumably at imaginary objects, for long periods. There is hyperesthesia to sound and touch with twitching of the ears or more general muscle fasciculation and tremors. Many throw their head sideways and show head shaking when the head or neck is touched. The predominant neurological signs are apprehensive behaviour, hyperesthesia and ataxia and a high proportion of cases lose body condition and have a diminishing milk yield during the clinical course of the disease. Other changes in temperament include the avoidance of other cows in loose housing but antagonistic behavior to herd mates and humans when in confined situations. Affected animals may kick during milking and show resistance to handling
The clinical course is variable

Meat and bone meal and the introduction of feed bans.

The initial epidemiological studies in Great Britain in 1997 suggested that the disease was an extended common source epidemic and the only common source identified in

these initial studies was the feeding of proprietary concentrate feedstuffs. Epidemiological studies subsequently identified meat and bone meal as the source of infection. The marked fall in disease incidence following the introduction of the feed ban has substantiated the importance of ingestion of contaminated meat and bone meal as the method of infection. In 1988 the UK Government introduced legislation which required all cattle suspected of suffering from BSE to be destroyed and sent for diagnosis. A ban on the feeding of ruminant meat and bone meal to ruminants was imposed in 1988. This initial ban was only on the feeding of ruminant protein to ruminants -ruminant protein could still be fed to pigs and poultry. It was subsequently recognized that that there could be cross contamination of feedstuffs in feed mills and/or feed trucks, and this, coupled with the recognition that a very small infective dose of infected brain could produce disease, led to the total ban in the UK in the 1990's on the feeding of all animal protein to farm animals and the mandatory recall of any meat and bone meal still present on farms. These procedures are resulting in the resolution of this disease in Great Britain (Fig 1) (Fig 2).

Infectivity in BSE

Challenge of cattle with sequential slaughter has detected infectivity in the terminal small intestine and tonsils (not detected in natural cases) and also in the brain, spinal cord, retina and dorsal root ganglia. Infectivity has not been detected in muscle meat, blood or in milk. It has not been detected in cattle less than 30 months of age.

Origin of the disease

There has been debate as to whether the transmissible agent is a strain of scrapie (a TSE of sheep and goats) that has modified to infect cattle or whether it originated from cattle. The agent and its pathology have characteristics that distinguish it from conventional scrapie strains and conventional scrapie, known for centuries, has never shown as a zoonotic disease. The mass exposure of cattle in Great Britain to the BSE agent, and the subsequent development of a disease epizootic in cattle in the latter half of the 1980s and the early 1990s is believed to have been the consequence of a change in the method of processing of meat and bone meal prepared from slaughter sheep (or cattle) latently infected with the agent so as to allow it to persist in this feed. Subsequent recycling of the agent in meat and bone meal prepared from latently infected slaughter cattle amplified its occurrence. There is also a theory that it was imported with bone meal from Africa. The source will probably never be determined conclusively.

Other species infected with the BSE agent.

Spongiform encephalopathies have been identified in seven species of ungulates in zoos or wildlife parks in Great Britain since the occurrence of the disease in cattle. These animals had been fed meat meal but the apparently shorter incubation period suggests that they might be more susceptible to infection than cattle and there is evidence for horizontal transmission in these species. BSE is transmissible by feed to domestic cats and a number of zoo species, including primates. It is transmissible to pigs by intracerebral inoculation but not by oral feeding. There have been no cases in poultry or dogs.

BSE in countries other than Great Britain.
The international trade in meat and bone meal, and possibly infected animals prior to the recognition of the disease has resulted in disease in other countries (Table 1). In some instances these countries did not admit to the occurrence and institute feed bans until some years after cases first occurred. It is quite probable that the disease is also in countries that are not reporting the disease or who do not have the surveillance structure to detect it.

New variant Creutzfeldt –Jakob disease.
Sub acute spongiform encephalopathies occur in humans (kuru, Creutzfeldt Jakob disease and Gerstmann Straussler Scheinker syndrome) and the occurrence of a new spongiform encephalopathy in a species used for human food resulted in considerable debate on the risk to human health and concern in the late 1980s in Great Britain. This fear proved correct and the BSE can affect humans who eat infected meat products and the disease has been named New variant Creutzfeldt –Jakob disease (vCJD). It has a different age of onset and different clinical course to classic Creutzfeldt Jakob disease. The number of cases to date is low, although still distressing. The figures for GB are shown in Fig 3. Year 2004 is to June 2004 and incomplete. A small number of cases (not shown) have been reported from European countries.

BSE in USA
The USA imposed a ban on the feeding of ruminant protein to ruminants in 1997. Providing there is compliance, this is the single most important firewall against the occurrence of BSE in the US.
There has been a passive surveillance of the brains of downer animals and cattle with neurological disease (rabies suspects that have proved negative for rabies, diagnostic laboratory submissions) for many years without BSE being detected until its detection in a cow in December 2003. The cow had originated from Canada and was born prior to Canada ban on meat and bone meal feeding of cattle – also in 1997. USDA's BSE surveillance program historically has been focused on the cattle populations where it is most likely to be found, including those condemned at slaughter because of signs of central nervous system disorders, non-ambulatory cattle and those that die on farms. In FY 2004, USDA sampled 20,543 animals—a sample size designed to detect the disease if it occurred in one animal per million adult cattle with a 95 percent confidence level, which is 47 times the international standard for low-risk countries.

The detection of a case of BSE and public and international concern has led to an enhanced testing program which started in June of this year. The goal of the program is to test as many cattle from the high-risk population as possible in a 12- to 18-month period. In order to reach as many high-risk cattle as possible, samples will be taken from the farm, slaughter facilities, rendering facilities, livestock auctions, veterinary clinics, and public health laboratories. The testing program will also randomly sample apparently normal, aged animals. The sampling of apparently normal animals will come from the 40 U.S. slaughter plants that handle 86 percent of the aged cattle processed for human consumption each year in the United States. Under the enhanced program, using statistically geographic modeling, sampling some 268,000 animals would allow for the

detection of BSE at a rate of 1 positive in 10 million adult cattle with a 99 percent confidence level. Rapid tests are conducted at selected diagnostic laboratories (one is the Washington Animal Diseases diagnostic laboratory). As of Mon 2 Aug 2004, the USDA had conducted 28 812 tests. 2 of the rapid tests were inconclusive, but immunohistochemistry conducted at Ames ruled out BSE.

Test results, posted on a weekly basis can be found at http://www.aphis.usda.gov/lpa/issues/bse_testing/test_results.html. Currently an ANPRM (advanced notice of proposed rule making) is requesting comments on the following measures related to animal feed, which is regulated by FDA:

1. removing specified risk materials (SRM's) from all animal feed, including pet food, to control the risks of cross contamination throughout feed manufacture and distribution and on the farm due to misfeeding;
2. requiring dedicated equipment or facilities for handling and storing feed and ingredients during manufacturing and transportation, to prevent cross contamination;
3. prohibiting the use of all mammalian and poultry protein in ruminant feed, to prevent cross contamination; and
4. prohibiting materials from non-ambulatory disabled cattle and dead stock from use in all animal feed.

Figure 1

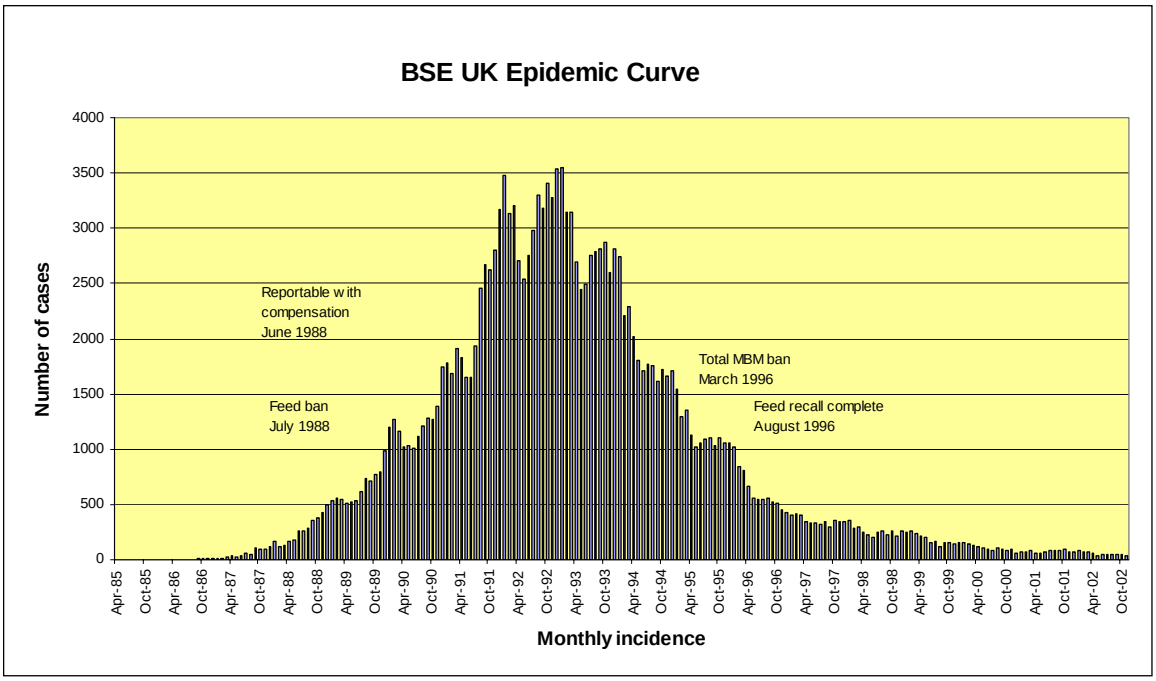
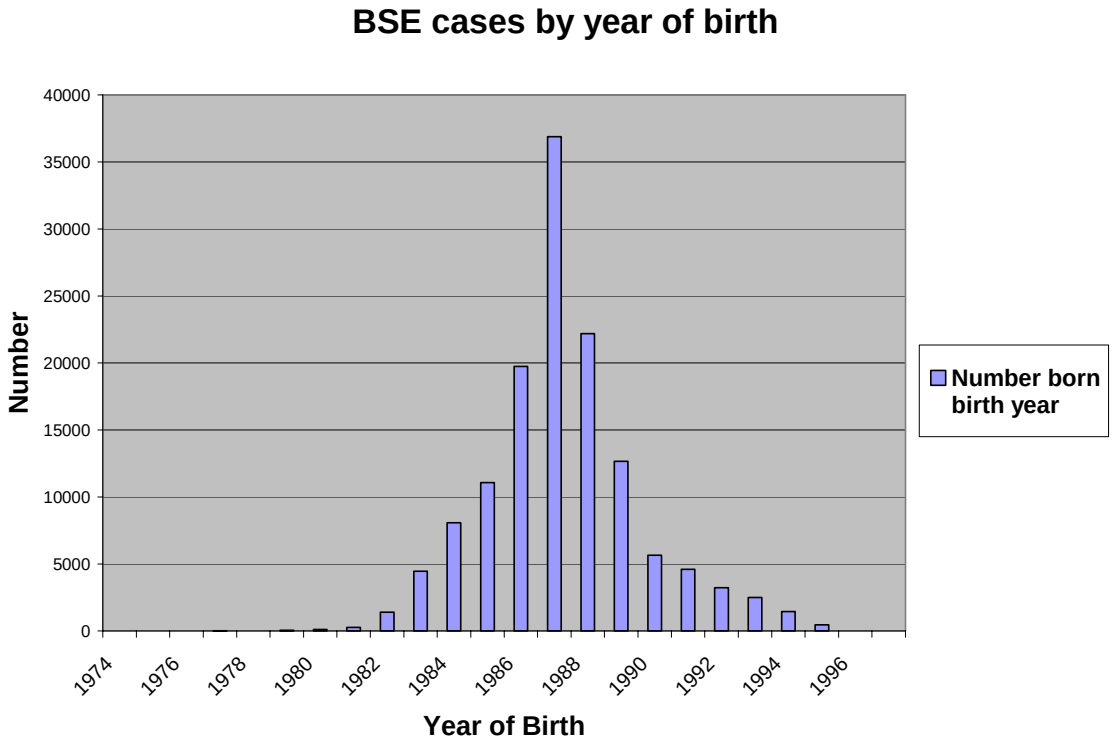


Figure 2


BSE cases by year of birth
40000
35000
30000
25000
20000
15000
10000
5000
0
Number
1974
1976
1978
1980
1982
1984
1986
1988
1990
1992
1994
1996
Year of Birth
Number born birth year

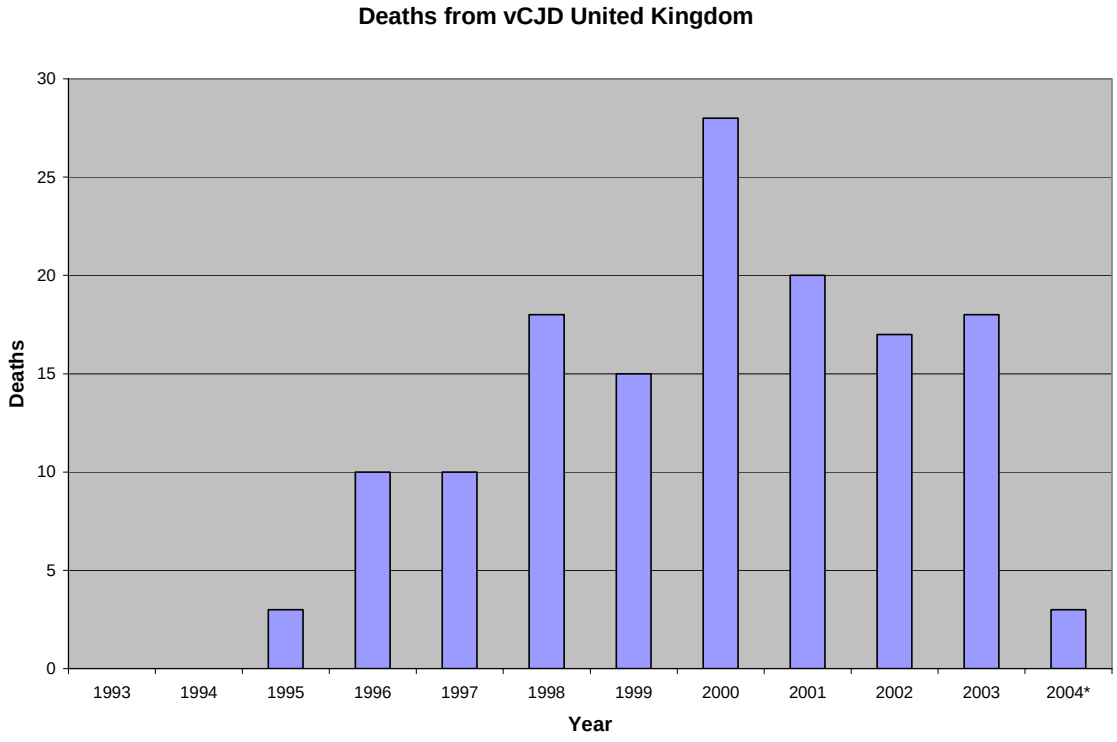

Deaths from vCJD United Kingdom
30
25
20
15
10
5
0
Deaths
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004*
Year

Table 1

BSE Cases. 2001 - July 2004 by Country					
Country	**2001**	**2002**	**2003**	**2004 to July**	**Total since 1987**
UK	1202	1144	612	103	183,906
Ireland	246	333	183	71	1424
France	274	239	137	32	924
Portugal	110	86	133	44	902
Spain	82	127	167	60	455
Switzerland	42	24	21	1	454
Germany	125	106	54	35	333
Belgium	46	38	15	8	125
Italy	48	38	29	3	120
Netherlands	20	24	19	5	76
Poland	0	4	5	7	16
Slovakia	5	6	2	3	16
Denmark	6	3	2	1	13
Czech Rep	2	2	2	4	12
Japan	3	2	4	2	11
Slovenia	1	1	1	1	4
Liechtenstein	0	0	0	0	2
Luxembourg	0	1	0	0	2
Austria	1	0	0	0	1
Canada	0	0	1	0	2
Finland	1	0	0	0	1
Greece	1	0	0	0	1
Israel	0	1	0	0	1
USA	0	0	0	1	1