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# The epidemics of bovine spongiform encephalopathy and variant Creutzfeldt–Jakob disease: current status and future prospects

Peter G. Smith<sup>1</sup>

**Abstract** The large epidemic of bovine spongiform encephalopathy (BSE) in the United Kingdom has been in decline since 1992, but has spread to other countries. The extensive control measures that have been put in place across the European Union and also in Switzerland should have brought the transmission of BSE under control in these countries, provided that the measures were properly enforced. Postmortem tests on brain tissue enable infected animals to be detected during the late stages of the incubation period, but tests that can be performed on live animals (including humans) and that will detect infections early are urgently needed.

The number of infected animals currently entering the food chain is probably small, and the controls placed on bovine tissues in the European Union and Switzerland should ensure that any risks to human health are small and diminishing. Vigilance is required in all countries, especially in those in which there has been within-species recycling of ruminant feed. Fewer than 150 people, globally, have been diagnosed with variant Creutzfeldt–Jakob disease (vCJD), but there are many uncertainties about the future course of the epidemic because of the long and variable incubation period. Better control measures are necessary to guard against the possibility of iatrogenic transmission through blood transfusion or contaminated surgical instruments. These measures will require sensitive and specific diagnostic tests and improved decontamination methods.

**Keywords** Encephalopathy, Bovine spongiform/epidemiology/etiology/prevention and control; Creutzfeldt-Jakob syndrome/epidemiology/etiology/prevention and control; Disease outbreaks/prevention and control; Cattle; Sheep; Animal feed/adverse effects; Disease transmission; Forecasting; United Kingdom; Switzerland; European Union (*source: MeSH, NLM*).

**Mots clés** Encéphalopathie bovine spongiforme/épidémiologie/étiologie/prévention et contrôle; Syndrome de Creutzfeldt-Jakob/épidémiologie/étiologie/prévention et contrôle; Epidémie/prévention et contrôle; Bovin; Mouton; Nourriture animale/effets indésirables; Transmission maladie; Prévision; Royaume-Uni; Suisse; Communauté économique européenne (*source: MeSH, INSERM*).

**Palabras clave** Encefalopatía espongiforme bovina/epidemiología/etiología/prevención y control; Síndrome de Creutzfeldt-Jakob/epidemiología/etiología/prevención y control; Brote de enfermedades/prevención y control; Bovinos; Ovinos; Alimentación animal/efectos adversos; Transmisión de enfermedad; Predicción; Reino Unido; Suiza; Unión Europea (*fuentes: DeCS, BIREME*).

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*Voir page 129 le résumé en français. En la página 129 figura un resumen en español.*

## Introduction

Variant Creutzfeldt–Jakob disease (vCJD) has so far been diagnosed in fewer than 150 people. The epidemic has attracted considerable attention, which, in terms of global threats to public health, some might consider to be disproportionate to its size. There are several reasons for such attention. First, vCJD appears to be a new disease. Second, although the present number of cases is small, the average incubation period is not known — it may be more than 10 years, and therefore many more people may be diagnosed in the coming years. Third, the disease is widely thought to be caused by a relatively newly recognized class of infectious agent, the prion, which has several notable characteristics — not least its ability to survive sterilizing processes that inactivate most biological agents. Fourth, the disease has predominantly affected young people, and its clinical course is relentless. The

disease is currently untreatable, very distressing, and uniformly fatal. Fifth, a high proportion of the United Kingdom population, as well as visitors to the country and people who have consumed bovine products exported from the United Kingdom, may have been exposed to the agent. Sixth, the epidemic of bovine spongiform encephalopathy (BSE) has had a substantial impact on world trade and has raised concern about the safety of a widely consumed food product, beef. Seventh, in the United Kingdom alone, the cost of the BSE epidemic has exceeded US\$ 6 billion, and substantial additional costs will continue to be incurred in the future, not least in guarding against the possibility of iatrogenic transmission of vCJD.

This review summarizes the evolution of the bovine and human epidemics, speculates on their future development, and summarizes some of the outstanding issues.

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## Origins of the BSE epidemic

Although the first case of BSE was identified in the United Kingdom in 1986, it is likely that some cases occurred earlier than this but were not detected and that the origin of the epidemic probably dates back to the 1970s. What caused the first case of BSE, why the epidemic started in the United Kingdom, and why it started when it did are questions that are unresolved and may remain so. What is clearer, however, is that the epidemic was caused by the practice of feeding cattle the waste parts of other cattle, which were not used for human consumption, in the form of meat and bone meal (MBM) after the bovine material had been rendered (1, 2). Rendering is the process whereby the waste parts of cattle are heated to separate out the fat and protein, so that the latter can be incorporated into MBM, a high-protein supplement feed. Studies showed that the rendering processes that were in use in the 1970s and 1980s in the United Kingdom, and in many other countries, may not have completely inactivated the infective agent (3).

Once the BSE agent had been introduced into this recycling process that transferred it from bovine to bovine, cases increased in number to cause the epidemic of the disease in the United Kingdom. In many respects, there are similarities with the epidemic of kuru (a human form of transmissible spongiform encephalopathy (TSE)) that affected several thousand people in a remote tribe in Papua New Guinea (see below).

Although it is reasonably certain that MBM caused the epidemic in the United Kingdom once the infective agent had entered cattle, how the infective agent got into cattle in the first place is far less clear. There are many competing hypotheses but two of the most plausible are that the initial case arose: sporadically in a bovine, and that tissue from this animal entered the rendering process (consequently, the infective agent was transferred to other cattle through feed); or through a cattle-adapted strain of the sheep TSE, scrapie, which entered the rendering process in the waste parts of a sheep (as sheep waste was also rendered and incorporated into MBM).

It is possible that BSE occurs sporadically in cattle at a very low frequency. This has never been documented, however, but if it is rare it might have been missed. Cases of the most common form of the human transmissible spongiform encephalopathy, CJD, appear to occur sporadically in old people at a very low incidence (1–2 per million per year). These cases may arise as a result of an endogenous process rather than by some environmental trigger. A plausible explanation for the origin of the epidemic of kuru in Papua New Guinea is that a sporadic case of CJD arose in the tribe around 1900 and the infective agent was passed to others through the cannibalistic funeral rituals practised by the tribe when that person died (4–6). The hypothesis of a “sporadic” case of BSE, however, does not explain why the disease occurred in the United Kingdom rather than elsewhere, given that the rendering and recycling processes that were prevalent in the United Kingdom were also in use in many other countries. It might have been a chance occurrence that BSE arose in this way when and where it did.

Scrapie has been endemic in sheep populations of the United Kingdom and other countries for centuries, and there is no evidence that it has caused disease in humans. However, multiple strains of scrapie have been identified, and it is possible that BSE is a modified form of one of these strains, or that it is a strain of scrapie that occurs in sheep at very low

frequency. In either case the strain could have been introduced into cattle through the rendering process, but again this hypothesis does not explain why the epidemic began in the United Kingdom or why it occurred in the 1970s or early 1980s, as MBM had been used for many years before this. One explanation originally proposed was that the ratio of sheep to cattle entering the rendering processes was higher in the United Kingdom than in most other countries, so that there was potentially a high concentration of the scrapie agent in MBM from the United Kingdom. Furthermore, changes to rendering processes were made around 1980 that may have reduced their capacity to lower the infectivity of scrapie agents (2). More recently, evidence has emerged that the United Kingdom was one of the first countries, in the 1970s, to start feeding MBM to very young calves and there is some evidence that young animals may have increased susceptibility to BSE (7).

## Impact of control measures

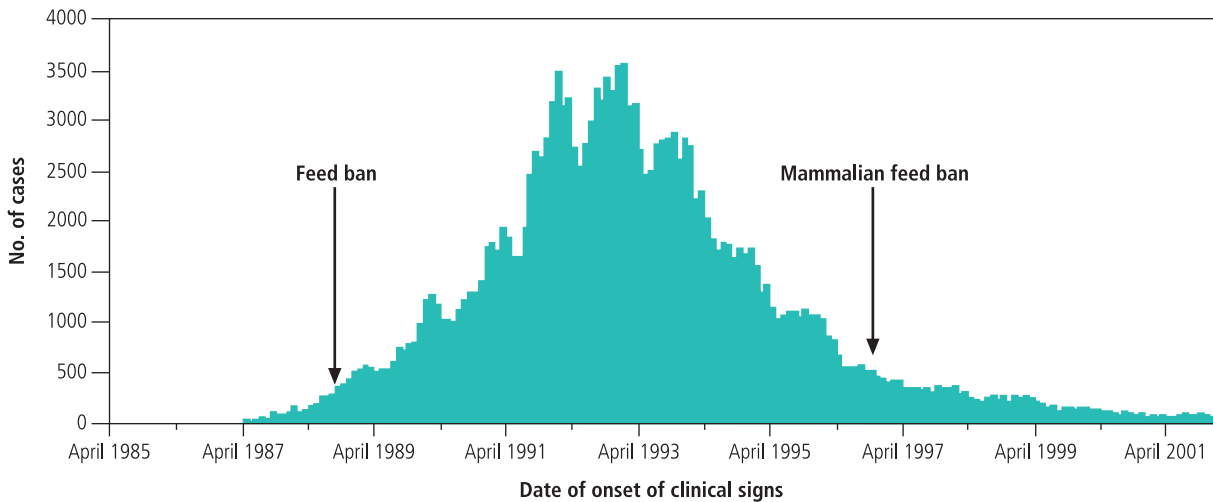
Epidemiological studies that were conducted shortly after the recognition of the BSE epidemic implicated MBM as the probable vehicle of transmission. Control measures banning the feeding of ruminant protein to ruminants were put in place in the United Kingdom in 1988, although at that time ruminant protein was still allowed to be fed to pigs and poultry because they were not thought to be susceptible to infection with the BSE agent. These control measures had a major impact on the epidemic, but it was not immediately apparent because of the long incubation period associated with the infection: animals were probably infected during their first year of life but the disease only manifested, on average, four or five years later. Fig. 1 shows the epidemic curve of the dates of onset of BSE cases in Great Britain. The peak of the epidemic occurred four to five years after the introduction of the ruminant feed ban, consistent with cattle being infected early in life.

Although the feed control measures seemed to have had a major impact on the epidemic (8), they were not as effective as had been hoped, and the disease continued to manifest itself in animals born after the measures had been introduced. This can be seen in Fig. 2, which is based on the same data as Fig. 1 but shows dates of birth of cases rather than dates of onset of BSE. It seems reasonable to attribute the sharp decline of BSE in animals born in 1988 and later to the introduction of the feed ban, but over 40 000 cases have now been reported in animals born after the date of the ban. There are several reasons for this, including a failure to recall feed initially, and “leakage” of feed intended for pigs and poultry back to cattle by several routes (9). Such feed was also exported and probably contributed to the occurrence of BSE in other countries.

Various measures were taken to strengthen the feed ban in the United Kingdom in the early 1990s and, following the report of the first cases of vCJD in 1996, a total ban was placed on feeding mammalian protein to any farmed animals and existing feed stocks from farms were recalled. It was hoped that this would totally close off the feed route that had fuelled the epidemic. The ban was essentially the same as the feed ban that was introduced across the European Union and in Switzerland in 2001, five years later.

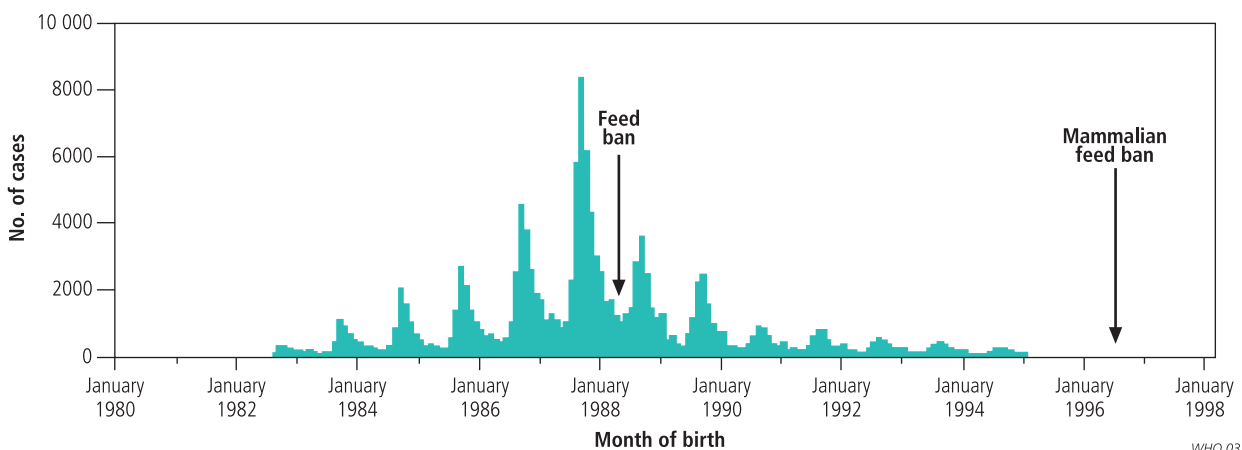
Advances in knowledge about the epidemiology of BSE have been hampered by the absence of a diagnostic test that can be applied to live animals to detect those that are incubating the infection. As a result, mathematical models of the epidemic

Fig. 1. Distribution of cases of bovine spongiform encephalopathy (BSE) in Great Britain, by date of onset of clinical signs



WHO 03.6

Fig. 2. Distribution of cases of bovine spongiform encephalopathy (BSE) in Great Britain, by month of animal's birth



WHO 03.7

have been used to estimate the numbers of animals infected at different times and to predict the impact of control measures on the evolution of the epidemic. Such modelling has indicated, for example, that in order to have observed 180 000 cases of BSE in the United Kingdom, about a million animals would need to have been infected (10). This is because most animals are slaughtered for human consumption at an age before BSE would have become clinically apparent. However, more recent work by this group has indicated that the number of infected animals may have been substantially higher than their original estimate (11). On the basis of such mathematical modelling it was expected that a small number of animals with BSE would be born after mid-1996 — even if the mammalian feed ban had been totally effective — because the feed ban would not have affected cases of BSE that were due to maternal transmission. It is not certain whether this route of transmission exists, but epidemiological studies have indicated that there might be a 10% risk of such transmission to calves born within six months of clinical onset of BSE in the dam (12, 13). The additional control measure that was introduced — the culling of the offspring of animals with BSE — should have

eliminated many of these cases, but would not have been effective for calves born to dams slaughtered shortly before BSE would have become clinically manifest. Thus, a small number of cases of BSE would have been expected in cattle born after 1996, whose dams had been culled or had died within six months of the calf's birth.

The number of cattle in which the onset of BSE occurred during 1999 to 2001 and that were born after mid-1996 was within the confidence bound of the number predicted due to maternal transmission from the mathematical model. The total number in the United Kingdom (up to January 2003) stands at 34. However, it seems unlikely that many of these cases can be explained by maternal transmission around the time of onset in the dams, as the dams of most of these animals have survived far beyond six months after giving birth — so far, with no evidence of having had BSE. Ongoing epidemiological investigations are trying to find clues to the origin of these cases. These studies are not easy because they involve investigating what happened to animals five to six years previously. In view of the partial success of the 1988 feed ban, the favoured hypothesis must be that the cases of BSE in cattle

born after mid-1996 are due to some residual leakage of contaminated feed, through a route yet to be identified (14). However, we cannot exclude the possibility of other routes of transmission that have been of minor importance in the past, but which are now more evident as the feed route has been finally closed off. Importantly, the number of infected cattle born after mid-1996 remains low and has not been increasing at a fast rate, at a time when animals in the 1996–97 cohort are at a peak-risk age for clinical BSE. Also, many of these cases have been identified by specific postmortem testing for BSE, rather than by clinical detection. So, although the epidemic in the United Kingdom is not over yet, the number of cases has declined consistently since 1992 and most cases that are now being reported are of animals born before 1996.

### Spread of BSE outside the United Kingdom

Although BSE was first identified in the United Kingdom, it has since been reported in many other countries, mostly in Europe. It is highly plausible that the epidemics of BSE in other European countries were seeded either by cattle exported from the United Kingdom that were incubating BSE or by the export of MBM contaminated with the BSE agent. However, rendering processes that were similar to those prevalent in the United Kingdom were also practised in other European countries. Once the infection had been introduced into cattle, it seems likely that it was recycled to other cattle through MBM in the same way as in the United Kingdom. Because, in general, control measures on feed were put in place later outside the United Kingdom, the epidemic curves for other countries have taken on a different shape. For example, the peak of the United Kingdom epidemic was in 1991, but occurred much later in other countries (see Fig. 3). Some cautions have to accompany Fig. 3. First, the United Kingdom data have been divided by 1000 so that all the curves could fit on the same scale. Second, most of the cases in the United Kingdom have been detected by identifying clinical cases of BSE, whereas a high proportion of cases in other European countries have been detected from

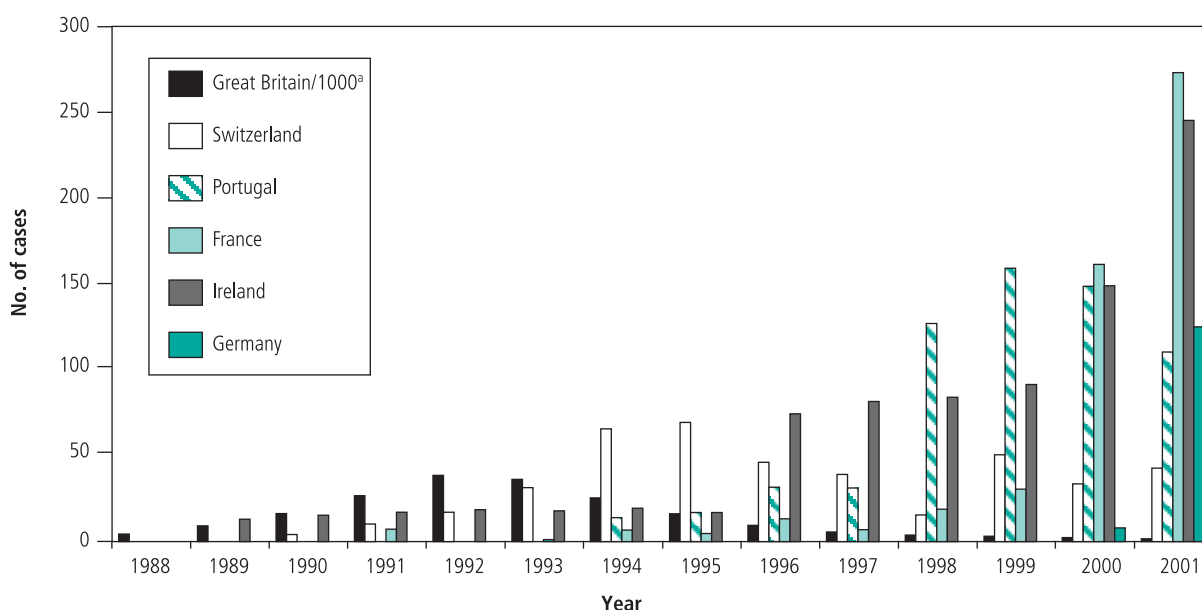
the large-scale testing programmes that have been put in place for all cattle aged over 30 months entering the food chain. However, these cautions do not detract from the main point shown in Fig. 3: the peaks of the epidemics occur at different times in different countries resulting from the impact of the different times that restrictions were put on feed in different European countries and the rigour with which they were enforced. The measures taken in different countries have been reviewed and assessed by various Scientific Committees of the European Commission (see [http://europa.eu.int/comm/food/fs/sc/ssc/outcome\\_en.html#opinions](http://europa.eu.int/comm/food/fs/sc/ssc/outcome_en.html#opinions)). As mentioned above, the 1996 ban on the feeding of mammalian protein to all farmed animals that was put in place in the United Kingdom was only implemented throughout the European Union from January 2001. These measures, if correctly enforced, should have eliminated transmission, or at least drastically reduced it. However, it will be some years before the full impact will be manifest in the decline in detected cases of BSE because of the long incubation period of the disease.

MBM that was contaminated with the BSE agent was probably exported from the United Kingdom to numerous countries, including some outside the European Union and Switzerland. It is therefore important that surveillance systems for BSE are strengthened and sustained in these countries, although the likelihood of a sustained epidemic depends largely on whether or not there has been recycling of ruminant protein to ruminants within those countries — a practice that is more common in industrialized countries. Such recycling has inherent risks for causing and spreading TSE and should be avoided.

### The human epidemic

The transmission of TSE agents between animals of the same species is generally easier to achieve than cross-species transmission and, for example, people have been eating scrapie-infected sheep for centuries with no evidence of ill effect. The BSE agent was thought most likely to be a cattle-

Fig. 3. Distribution of cases of bovine spongiform encephalopathy (BSE) in various European countries



<sup>a</sup>Data for Great Britain are divided by 1000

adapted form of the scrapie agent. In the early years of the BSE epidemic these factors led to the view that it was unlikely that humans would be infected with BSE. Nonetheless, precautionary measures were put in place: bovine tissues that were likely to have high titres of the infectious agent — in particular, brain and spinal cord — were banned from the human food chain. Also, in 1990, a national surveillance unit for CJD was set up in the United Kingdom because any presentation of BSE in humans was thought likely to resemble CJD.

Concern that BSE may have crossed over into the human population was heightened in 1995 when CJD was identified in two teenagers — an age group in which CJD has rarely been reported — in the United Kingdom. These cases were followed in 1995 and early 1996 by more cases of CJD in young people; the neuropathology was found to be very similar in these patients but distinctly different from that previously observed for CJD (15). This new variant of CJD (now designated vCJD) was thought most likely to be caused by infection with the BSE agent, largely on the grounds of biological plausibility. The United Kingdom Government announced the possible link between BSE and vCJD in March 1996, and this was followed by a worldwide ban on British beef products. Further precautionary measures in the United Kingdom included banning cattle over the age of 30 months from the human food chain — a control measure that remains in place today. In 1996, the epidemiological evidence supporting the link between BSE and vCJD was not strong. It consisted, essentially, of the knowledge that BSE and vCJD appeared to be confined to the United Kingdom and that an incubation period of 5–10 years was not inconsistent with that observed following iatrogenic transmission of “classic” CJD after the use of contaminated human growth hormone (16). Questioning the relatives of patients with vCJD about the dietary habits of the patients (and their occupations, places of residence, and exposure to medical procedures) established no marked differences from those of people without the disease. Perhaps this was not surprising, given that the agent may have been distributed in a variety of beef products, which were consumed by most of the population, and that the people may have been exposed to the causative agent a decade or more previously. It was not until a year or so later that it was established beyond reasonable doubt that vCJD and BSE were caused by agents that were indistinguishable (17, 18). The route of transmission to humans remains unclear, but cattle and sheep can be infected experimentally by the oral route and the most plausible explanation for the human cases is from dietary exposure. Why the disease affects predominantly young people is currently not understood.

Because of the probable widespread exposure of the United Kingdom population to contaminated beef products, there were initial fears that the vCJD epidemic in humans may be very large. Although the possibility of a large epidemic still cannot be completely excluded, the number of cases has not grown at the rate that some feared (Table 1). Because there is currently no diagnostic test that reliably identifies people incubating vCJD, and because the average incubation period may be very long, it has been impossible to predict the ultimate size of the epidemic with any confidence. Various research groups have attempted to build mathematical models to investigate possible scenarios, and current best estimates indicate that the epidemic may affect fewer than 1000 people (19–21). However, the confidence limits on estimates are wide

Table 1. Distribution of cases of variant Creutzfeldt–Jakob disease in the United Kingdom<sup>a</sup> up to January 2003

Year person died	No. of cases
1995	3
1996	10
1997	10
1998	18
1999	15
2000	28
2001	20
2002	17
Total deaths	121 <sup>b</sup>
Cases alive	8
Total cases	129

<sup>a</sup> Cases outside the United Kingdom: 6 in France; 1 in Ireland; and 1 in Italy. There has also been 1 case in the USA and 1 case in Canada of people who had previously lived in the United Kingdom in the 1980s and early 1990s.

<sup>b</sup> Includes 27 without neuropathological confirmation.

and, although hundreds of thousands of cases seem unlikely, some researchers are unwilling to exclude the possibility of tens of thousands of cases (21), whereas others have put the limit an order of magnitude lower (19, 20). This modelling has been done with few data inputs, and some important assumptions have been imposed. The models have not taken account of possible person-to-person transmission — for example, through blood transfusions or from contaminated surgical instruments. Furthermore, they have assumed that the number of cases will continue to be restricted to approximately 40% of the population who are methionine homozygous at codon 129 of the prion protein gene (as has been true with cases observed to date).

## Outstanding issues

The measures that were put in place to control the BSE epidemic in the United Kingdom have resulted in a year-on-year decrease of 25–45% in the annual number of BSE cases reported, and the epidemic is now essentially “under control”. The cases arising for animals born after mid-1996 are of some concern because their etiology is unclear. However, the cases are small in number and, given the control measures in place, it is unlikely that they will have a significant impact on animal or public health. As shown in Fig. 3, the much smaller epidemics in other European countries are at an earlier stage in their course than that in the United Kingdom. However, given that the mammalian feed ban has been in place across the European Union and in Switzerland since January 2001, these epidemics are expected to decline greatly in the birth cohorts born after that date. The control measures preventing high-risk bovine tissues from entering the human food chain substantially reduce the possible risks to human health. Furthermore, the testing for BSE of all animals over the age of 30 months that are slaughtered for human consumption provides an additional safety measure, as this will detect infected animals in the late stage of the incubation period. The recycling of bovine tissue in cattle feed was the underlying cause of the BSE epidemic, and maintaining controls on this should prevent BSE re-emerging as a veterinary health problem. This lesson applies, of course, even to countries that have had few or no cases of BSE.

Priorities for the future must include continuing to monitor the level of BSE-infected cattle and to enforce controls on high-risk tissues from entering the food chain.

In addition to the above, there are three outstanding issues that should be priorities for research and action in the future, as discussed below.

### Diagnostic tests

We still have little idea of how many people have been infected with the BSE agent and are incubating vCJD. The development of a diagnostic test that can be applied to a tissue that is easily sampled in life (e.g. blood) and that detects infection early in the incubation period is of the highest priority. Studies are under way in the United Kingdom to examine appendix and tonsil samples, removed during normal surgery, for evidence of infection with the vCJD agent (22). They may provide some data on the extent of human infection, although the interpretation of the results will be severely limited by the absence of knowledge of the sensitivity and specificity of the test procedures at different stages of the incubation period. Studies in sheep indicate that TSE agents may be detectable in tonsil samples early in the incubation period, and the same may be true for vCJD in humans, but this is not certain. So far, the agent has been consistently detected in the tonsils of vCJD cases after clinical onset of the disease (23). With a sensitive and specific diagnostic test it will be possible not only to make a better estimate of the extent of human infection but also to implement more focused control measures to guard against iatrogenic transmission. However, there are formidable ethical considerations in the deployment of such tests, which may be of uncertain sensitivity and specificity; for example, they might diagnose an infection at an unknown point in the incubation period of a disease that is fatal and currently untreatable.

### Iatrogenic transmission

More information on the possibility of iatrogenic transmission is urgently required. There have been several instances of iatrogenic transmission of CJD, mostly through the use of human grown hormone and dura mater grafts, and a few from contaminated neurosurgical instruments (16). Transmission of CJD by blood transfusion has not been documented (24), but because the pathogenesis of vCJD differs from that of CJD — in particular, in the role of the lymphatic system — the possibility of transmission of vCJD by this route is an important health concern, the more so since the recent demonstration that experimentally induced BSE in sheep could be transmitted by blood transfusion (25, 26). Because of the assumed association of the vCJD agent with white blood cells, leukodepletion of blood used for transfusions has been implemented in the United Kingdom. Also, in the United Kingdom pooled plasma products are now sourced from abroad in an attempt to reduce the theoretical risks from transmission by these routes. A diagnostic test to determine whether blood donors have been infected with the vCJD agent would potentially reduce the risk of transmission greatly by these routes.

Normal hospital autoclaving procedures do not completely inactivate the vCJD agent (27), and so it might be transmitted from patient to patient through the use of contaminated instruments. Such risks might be reduced by the greater use of single-use instruments, but this is unlikely to be feasible for all instruments because some are costly (e.g.

endoscopes), and there might also be other risks associated with the use of cheaper instruments, which single-use instruments are likely to be. A generic solution to this problem will be to develop sterilization procedures that can be routinely applied and that inactivate the agent, but which are not so severe as to damage the instruments. A substantial research programme is under way in this area.

### BSE in sheep

The possibility of BSE occurring in sheep is a further cause for concern. In the United Kingdom sheep were fed the same MBM that caused the BSE epidemic in cattle, albeit in considerably smaller quantities than were fed to cattle. However, less than 1 g of BSE-infected bovine brain fed experimentally to a sheep can cause BSE (28), and the disease presents clinically as indistinguishable from scrapie. There is no evidence of an epidemic of “scrapie” in sheep coincident with the BSE epidemic in cattle (29), but surveillance for scrapie is poor, and the possibility that some sheep have been infected with BSE cannot be excluded. The feed controls that were implemented to prevent transmission in cattle were also applied to sheep and, as sheep have a shorter lifespan than cattle, it is unlikely that any sheep infected through the feed route are still alive. However, scrapie has been maintained in the sheep flock for several centuries and, although the routes of transmission from sheep to sheep are uncertain, some form of horizontal transmission must occur. Such transmission of BSE in cattle is, at most, rare and has never been established. Thus, in sheep if BSE behaves like scrapie, it could have persisted in the sheep flock despite the imposition of feed controls (21, 30). Present methods of strain-typing, to distinguish BSE from scrapie in sheep, have not been fully validated. One method involves infecting inbred strains of mice by intracerebral injection and recording the incubation periods and patterns of brain lesions in the mice. Not only is this a very expensive method, but a single study takes 18 months or more to complete. So far, about 180 cases of scrapie have been studied by this method and none have shown BSE-like characteristics. However, this does not exclude the possibility that a small proportion (1–2%, the 95% upper confidence limit in observing 0 cases in 180 tested) of cases of scrapie may be attributable to the BSE agent. Urgent priority is being given to developing molecular methods of diagnosis that will permit the rapid differentiation of BSE and scrapie strains. Although high levels of BSE infectivity are confined to a few tissues in cattle, the distribution of the BSE agent is much more widespread in sheep that have been experimentally infected with it. Therefore, banning specific sheep tissues from the diet would be a more difficult control option in preventing possible transmission to humans.

### Conclusions

It might not be possible to assess the full impact of the BSE epidemic on human health for many years. It is likely that millions of individuals have been exposed to contaminated beef products in the United Kingdom, but, to date (January 2003), only 139 cases of vCJD have been ascertained. Perhaps the cattle-to-human species barrier for transmission of the infective agent is very high, such that the total number of cases will remain small. However, we cannot exclude at this stage that the incubation period is very long — possibly several decades on average — and that the peak of the human

epidemic is yet to come. The number of cases outside the United Kingdom is still small (Table 1). The source of the infection for these cases is unknown, but it is plausible, for example, that most — if not all — of the cases in France owe their origin to contaminated meat or meat products exported from the United Kingdom (31).

There seem to be good grounds for optimism that the extensive control measures put in place have brought the transmission of BSE under control in the European Union and Switzerland. It is important to note, however, that cases of BSE will continue to arise in future years because of the long incubation period of the disease. A significant advance has been made in the development of postmortem tests, which can now be performed relatively rapidly and cheaply on brain tissue and enable infected animals to be detected in the late stages of the incubation period. These tests are now mandatory for all cattle entering the food chain aged over 30 months anywhere in the European Union, and massive testing programmes have been set up.

The evidence accumulated to date indicates that, although there has been an enormous BSE problem in the United Kingdom, the control measures put in place since 1988, and especially since 1996, have brought the epidemic well under control, and there is no good reason why the consistent decline seen over the past decade should not continue. The number of infected animals entering the food chain now is likely to be very small, and the controls placed on bovine tissue entering the market should ensure that any risks to human health will be very low and will diminish. It would be rash to predict when the last case of BSE will occur, but the disease in cattle is probably no longer a significant public health problem, and is unlikely to become so in the future, provided that appropriate controls are enforced. However, many challenges remain. ■

#### Acknowledgement

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**Conflicts of interest:** none declared.

## Résumé

### L'épidémie d'encéphalopathie spongiforme bovine et de nouvelle variante de la maladie de Creutzfeldt-Jakob : situation et perspectives

L'importante épidémie d'encéphalopathie spongiforme bovine (ESB) au Royaume-Uni est en recul depuis 1992, mais s'est étendue à d'autres pays. Les mesures de grande envergure mises en place dans l'Union européenne et également en Suisse, si elles avaient été correctement appliquées, auraient pu endiguer la transmission de l'ESB. Les tests post-mortem sur le tissu cérébral permettent de détecter la maladie au cours des derniers stades de la période d'incubation chez les animaux infectés, mais il est urgent de disposer de tests réalisables sur le vivant chez l'animal comme chez l'homme pour détecter les infections à un stade précoce.

Actuellement, le nombre d'animaux infectés entrant dans la chaîne alimentaire est probablement faible et les contrôles effectués sur les tissus bovins dans l'Union européenne et en

Suisse doivent assurer que les risques éventuels pour la santé humaine sont faibles et en voie de diminution. La vigilance est requise dans tous les pays, en particulier ceux où il y a eu recyclage des aliments pour ruminants d'une espèce à l'autre. Moins de 150 personnes dans le monde ont fait l'objet d'un diagnostic de nouvelle variante de la maladie de Creutzfeldt-Jakob, mais il reste de nombreuses incertitudes quant à l'évolution future de l'épidémie du fait de la durée et de la variabilité de la période d'incubation. De meilleures mesures de lutte sont indispensables pour éviter la transmission iatrogène lors de transfusions sanguines ou par le biais d'instruments chirurgicaux contaminés. Ces mesures nécessiteront des tests diagnostiques sensibles et spécifiques et des méthodes de décontamination plus efficaces.

## Resumen

### Epidemias de encefalitis spongiforme bovina y de la nueva variante de la enfermedad de Creutzfeldt-Jakob: situación actual y perspectivas

La importante epidemia de encefalopatía spongiforme bovina (EEB) sufrida por el Reino Unido viene remitiendo desde 1992, pero se ha extendido a otros países. Las medidas generalizadas de control implantadas en toda la Unión Europea y en Suiza deberían haber permitido frenar la transmisión de la EEB si se hubieran aplicado estrictamente. Las pruebas postmortem practicadas en el tejido cerebral permiten detectar la enfermedad en los animales infectados durante las últimas fases del periodo de incubación, pero se necesitan urgentemente pruebas aplicables a animales vivos (incluido el ser humano) que detecten tempranamente la infección.

El número de animales infectados que llegan actualmente a la cadena alimentaria es probablemente pequeño, y los controles a que se somete a los tejidos bovinos en la Unión Europea y en Suiza

llevan a pensar en principio que, si algún riesgo hay para la salud humana, debe de ser pequeño y con tendencia a desaparecer. Es preciso mantener la vigilancia en todos los países, especialmente en aquellos en los que ha habido reciclaje de piensos para ruminantes en el interior de una misma especie. A nivel mundial, menos de 150 personas han sido diagnosticadas como afectadas por la nueva variante de la enfermedad de Creutzfeldt-Jakob, pero hay mucha incertidumbre respecto al curso futuro de la epidemia debido a lo extenso y variable del periodo de incubación. Se necesitan mejores medidas de control para proteger contra posibles transmisiones iatrogénicas por transfusión de sangre o instrumentos quirúrgicos contaminados. Estas medidas requerirán pruebas diagnósticas sensibles y específicas y mejores métodos de descontaminación.



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