A model to assess the risk of the introduction into Japan of the bovine spongiform encephalopathy agent through imported animals, meat and meat-and-bone meal

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Summary
The authors developed a mathematical model to assess the release risk of the bovine spongiform encephalopathy (BSE) agent into a country through the importation of live cattle, bone-in bovine meat and meat-and-bone meal (MBM) from the United Kingdom and other countries with BSE. Monte Carlo simulation was attempted using this model and input variables. The release risk in Japan, expressed as the weight of infected MBM released in Japan between 1993 and 2000, was estimated to be 23.4 kg to 53.8 kg. The simulation also indicated that imported MBM represented the most important risk factor for releasing the BSE agent into Japan. This paper also provides details of the first five cases of BSE detected in Japan between September 2001 and the end of 2002. In addition, the results of the investigation conducted to determine the source of infection and the measures taken by the Government of Japan to prevent the BSE agent from entering the food and feed chains are also outlined.

Keywords

Introduction
Bovine spongiform encephalopathy (BSE) is a fatal neurological disease of adult cattle with a long incubation period. There is no assurance that a country is free from BSE infection even if no case of BSE has been declared in that country. Cattle that have consumed feed containing meat-and-bone meal (MBM) contaminated with the BSE agent may become infected and develop clinical signs after an incubation period of four to six years, with a modal incubation period of sixty months. Therefore, countries which in the past possessed inadequate control measures to protect the cattle population from exposure to contaminated feed are at a higher risk of experiencing BSE in the future than countries in which effective measures were taken in the past for a period longer than the incubation period.

The Government of Japan has taken various measures to protect the cattle population from exposure to contaminated feed, mainly through import controls on live cattle and cattle products from countries with an incidence of BSE. In spite of these measures, the first case of BSE was detected in Japan on 10 September 2001, followed by a second, third, fourth and fifth case in November and December 2001, and May and August 2002, respectively.
This paper proposes a mathematical model to assess the risk of introduction of the BSE agent (release risk) into Japan through importation of animals, bone-in carcass meat and mammalian MBM.

The paper also describes the results of investigations to determine the source of introduction of the BSE agent, as well as measures taken to prevent the agent from entering into food and feed chairs, after detection of cases of the disease in Japan in 2001.

Materials and methods

Basic assumptions used in the release assessment

The application of this BSE release assessment method is based on the assumption that BSE arose in the United Kingdom (UK) and was propagated through the recycling of inadequately processed BSE-infected bovine tissues into animal feed. Later, exportation of infected animals, infected meat products and infected MBM provided the means for the possible spread of the BSE agent to other countries in Europe, with infected MBM being the source of infection for the animals in these countries.

Exports of contaminated products from these countries have led to further spread of the BSE agent to countries with no incidence of the disease.

Release assessment model

The release risk was assessed quantitatively by estimating the amount of infected MBM released following imports into Japan of infected live cattle, infected bone-in carcass meat and infected MBM between 1993 and 2000.

Based on scientific assessment, the authors considered that cattle semen and embryos can be imported safely without risking the introduction of BSE, and consequently did not include these imports as risk factors. This opinion is widely shared by experts having researched BSE (3, 4, 33, 40).

The authors considered that ruminant protein other than MBM (including meat meal, bone meal and blood meal) does not constitute a risk factor as significant as MBM and have not taken them into account in assessing the release risk.

Release risk arising from the import of infected animals

Figure 1 illustrates the scenario tree outlining the events and pathways which result in the release of infected MBM following the importation of live cattle. The authors assumed that the BSE agent is released when all of the following events occur:

- infected cattle are imported
- the infected cattle are transformed into MBM

- specified risk material (SRM) is not removed when infected animals are slaughtered
- material containing SRM is not processed at 133°C for 20 min. at 3 bar or with a method providing equivalent guarantees.

Regarding the last two events, coefficients were used to take into account the fact that SRM removal and rendering to the said standard do not absolutely guarantee removal and destruction of all BSE infectivity.

In Figure 1, the first pathway commencing with the event that a BSE-infected animal is culled or dies is represented by the formula $AB \times S \times (1 - COS) \times R \times (1 - COR)$. Combining all pathways leads to the following probability calculation:

$$RR_{animal}(kg) = \sum_{m=1}^{778} \sum_{n=17}^{1993} AN_{mn} \times P_{mn} \times (AB \times (1 - S \times COS) + RE) \times (1 - R \times COR) \times W_{MBM}$$

where:

- $AN_{mn} = \text{number of live cattle imported from country } m \text{ in the year } n$
- $P_{mn} = \text{BSE prevalence in country } m \text{ in the year } n$
- $AB_m = \text{probability that an animal imported in the year } n \text{ is sent to an abattoir}$
- $S_n = \text{probability that SRM is removed from an animal}$
- $COS = \text{efficiency of SRM removal}$
- $RE_n = \text{probability that an animal imported in the year } n \text{ is sent to a rendering plant}$
- $R_n = \text{probability that animal by-products are rendered by heat-treatment at } 133°C \text{ for } 20 \min \text{ at 3 bar}$
- $COR = \text{probability that heat-treatment at } 133°C \text{ for } 20 \min \text{ at 3 bar inactivates the BSE agent}$
- $W_{MBM} = \text{average weight of MBM from one animal (kg)}$

$m = 15 \text{ EU Member States, Switzerland and Liechtenstein}$

Release risk arising from the import of infected bone-in carcass meat

Figure 2 illustrates the scenario tree outlining the events and pathways which result in the release of infected MBM following the importation of meat products. The authors assumed that the BSE agent is released as the result of the importation of bone-in bovine meat, which may contain spinal cord and dorsal root ganglia, when all of the following events occur:

- bone-in meat of bovine origin from an infected animal is imported
- the SRM is not removed from infected bone-in carcass meat
- trimmings or scraps (bone, fat and SRM residues) generated from the bone-in carcass meat are sent for rendering into MBM
- bone-in carcass meat sent to a rendering plant is not subjected to heating at 133°C for 20 min. at 3 bar.

Regarding the second and the last events, coefficients are used to take into account the fact that SRM removal and heat-treatment at 133°C for 20 min. at 3 bar do not absolutely guarantee removal and destruction of all BSE infectivity. Meat products other than bone-in carcass meat are not assumed to constitute a risk factor as these products will not be rendered in any circumstances, while there is a chance that a significant proportion of bone-in meat (mainly bone and fat and possibly some SRM residue) is rendered.

In Figure 2, the first pathway commencing with the event that SRM is removed is represented by the formula

\[ \text{SME} \times (1 - \text{COS}) \times \text{SCR} \times (1 - \text{COR}) \times \text{MBM} \]

Combining all pathways leads to the following probability calculation:

\[ \text{SME} \times (1 - \text{COS}) \times \text{SCR} \times (1 - \text{COR}) \]

Fig. 1
Scenario tree outlining the events and pathways leading to the 'release' of infected meat-and-bone meal following importation of live cattle
Commencing with the event that bone-in meat of bovine origin from an infected animal is imported, and converting the output into the weight of infected MBM, the release risk, expressed as the expected weight of infected MBM released following the importation of infected meat products from 17 countries in Europe between 1993 and 2000 ($RR_{meat}$) is estimated as follows:

$$RR_{meat} (kg) = \sum_{m=1}^{17} \sum_{n=1993}^{2000} MEAT_{mn} \times 1000 \times W_{MEAT} \times P_{mn} \times SCR_n \times (1 - SME_{mn} \times COS) \times (1 - R_n \times COR) \times W_{MBM}$$

where:

- $MEAT_{mn}$ = amount of bone-in meat of bovine origin imported from country $m$ in the year $n$ (metric tonnes [MT])
- $W_{MEAT}$ = average weight of bone-in meat from one animal (kg)
- $P_{mn}$ = BSE prevalence in country $m$ in the year $n$
- $SCR_n$ = probability of generating scraps or trimmings that are rendered into MBM
- $SME_{mn}$ = probability that SRM is removed from an animal in producing bone-in meat in country of origin $m$ in the year $n$
- $COS$ = efficiency of SRM removal
- $R_n$ = probability that an animal is rendered by heat-treatment at 133°C for 20 min. at 3 bar in Japan in the year $n$
- $COR$ = probability that heat-treatment at 133°C for 20 min. at 3 bar inactivates the BSE agent
- $W_{MBM}$ = average weight of MBM produced from bone-in meat from one animal (kg)
- $M = 15$ EU Member States, Switzerland and Liechtenstein

**Release risk arising from the import of infected meat-and-bone meal**

Figure 3 illustrates the scenario tree outlining the events and pathways which result in the release of infected MBM following the importation of MBM. The authors assumed that the BSE agent is released as the result of importation of MBM (including
bone meal, meat meal and blood meal), when all of the following events occur:

– MBM from an infected animal is imported
– the SRM was not removed from an animal rendered for the production of MBM
– the MBM was not heat-treated at 133°C for 20 min. at 3 bar.

Regarding the last two events, coefficients are used to take into account the fact that SRM removal and treatment by heating at 133°C for 20 min. at 3 bar do not absolutely guarantee removal and destruction of all BSE infectivity.

In Figure 3, the first pathway commencing with the event that SRM is removed is represented by the formula

\[ \text{SMB} \times (1 - \text{COS}) \times \text{RMB} \times (1 - \text{COR}) \times (1 - \text{RMB}) \times (1 - \text{SMB}) \times (1 - \text{COS}) \times \text{RMB} \times (1 - \text{COR}) \times (1 - \text{RMB}) \],

which can be simplified to

\[ (1 - \text{SMB} \times \text{COS}) \times (1 - \text{RMB} \times \text{COR}) \times \text{W}_{\text{MBM}} \times \text{P}_{\text{mn}} \]

Commencing with the event that MBM from an infected animal is imported, and converting the output into the weight of infected MBM, the release risk, expressed as the expected weight of infected MBM released following the importation of infected MBM from 17 countries in Europe between 1993 and 2000 (RR_{mbm}) is estimated as follows:

\[ \text{RR}_{\text{mbm}}(\text{kg}) = \sum_{m=1}^{17} \sum_{n=1}^{8} \text{MBM}_{mn} \times 1000 \times \text{W}_{\text{MBM}} \times \text{P}_{\text{mn}} \times (1 - \text{SMB}_{mn} \times \text{COS}) \times (1 - \text{RMB} \times \text{COR}) \times \text{W}_{\text{MBM}} \]

where:

- \( \text{MBM}_{mn} \) = amount of MBM (including bone meal, meat meal and blood meal) imported from country \( m \) in the year \( n \) (MT)
- \( \text{W}_{\text{MBM}} \) = average weight of MBM from one animal (kg)
- \( \text{P}_{\text{mn}} \) = BSE prevalence in country \( m \) in the year \( n \)
- \( \text{SMB}_{mn} \) = probability that SRM is removed from an animal in producing MBM in country of origin \( m \) in the year \( n \)
COS = efficiency of SRM removal

\[ \text{RMB}_{mn} = \text{probability that animal by-products are heat-treated at } 133^\circ\text{C for 20 min. at 3 bar in country of origin } m \text{ in the year } n \]

COR = probability that heat-treatment at 133°C for 20 min. at 3 bar inactivates the BSE agent

\[ m = 15 \text{ EU Member States, Switzerland and Liechtenstein} \]


The total release risk, expressed as the expected weight of infected MBM released following the importation of live animals, meat products and MBM in the past eight years was estimated by aggregating the amounts of MBM released through each scenario, as follows:

\[ RR_{\text{total(kg)}} = RR_{\text{animal}} + RR_{\text{meat}} + RR_{\text{mbm}} \]

A stochastic model was employed to reflect the uncertainty of some of the values used for the input variables. The input variables were modelled as probability distributions and Monte Carlo simulation was used to combine the variables into an output distribution of probability estimates. The simulations were performed using @Risk software and an Excel 5.0 spreadsheet.

Five thousand iterations were run, and the results were summarised using percentile values, probability density and cumulative density functions.

**Input variables**

**Import data of animals, bone-in meat and meat-and-bone meal (AN\(_{mn}\), MEAT\(_{mn}\) and MBM\(_{mn}\))**

Import data of live cattle and bone-in meat from EU Member States, Switzerland and Liechtenstein between 1993 and 2000 used for estimation of the release risk are based on statistics issued by the custom authorities in Japan (1). During this period, live cattle were imported only from Germany and France: sixteen animals were imported from Germany in 1993 and eight animals imported from France in 1998. The eight cattle imported from France in 1998 were all shipped back after being used for an exhibition and therefore not considered in the release risk estimation. Import data of bone-in meat used for estimating the release risk are shown in Table I.

The MBM import data in Table II are based on Animal Quarantine Statistics issued by the Ministry of Agriculture, Forestry and Fisheries (MAFF) of Japan (19), and are the aggregate of MBM, bone meal, meat meal and blood meal derived from cloven-hoofed animals. Although a substantial amount (835 MT) of bone meal was imported from Ireland between 1991 and 1998, these products were confirmed, based on records kept by the Animal Quarantine Service and the importers, to be bone-meal for human consumption, imported as supplementary food, or crushed bone for the production of gelatine (29). The imports of bone meal from Ireland were therefore not taken into account in estimating the release risk.

**Proportion of infective animals in countries in Europe (P\(_{mn}\))**

Table III shows the proportion of infective animals used as input variables for the EU Member States from which any of the aforementioned products were imported into Japan between 1993 and 2000.

Although data is available from the OIE (World organisation for animal health) on the annual incidence of BSE in these countries between 1989 and 2001, these data are not reliable before 2001 when active surveillance was initiated in every EU Member State. The annual incidence of 2001 was therefore used to estimate the incidence in these countries in the preceding eight years.
The apparent annual incidence of BSE in Denmark in 2001 was 6.77 per million cattle (34). According to the Opinion of the Scientific Steering Committee of the European Commission (EC-SSC) on the geographical risk of BSE (GBR) in Denmark, the disease was prevalent in Denmark as early as in 1992 and would have increased until 1995 and then remained at the same level until 1997, decreasing slowly after that (9). The authors therefore considered that they would not either underestimate or overestimate the true incidence of the disease if they assumed that this value was nil in 1991, but gradually increased reaching peak incidence in 1995-1997, which is two to five times higher than the apparent incidence in 2001 and most likely three times higher, and then gradually declined to the current incidence.

In Germany, the apparent annual incidence in 2001 was 19.97 per million cattle (34). According to the EC-SSC, the cattle population of Germany was exposed to external challenges during the 1980s and the early 1990s and BSE infectivity was assumed to be amplified until 1996, after which year the anticipated amount of circulating BSE-infectivity is considered constant (11). The authors therefore assumed that true BSE incidence in Germany started to exist in 1990 and reached a peak in 1995, which is two to five times higher than the apparent incidence observed in 2001 and most likely three times higher, and then declined to the current level of incidence.

In Sweden, no cases of BSE had been detected at the time of writing this paper (34). According to the EC-SSC, BSE is unlikely to have entered the country and should this have been the case, disease prevalence would have remained very low and decreased slowly since 1997 (14). The authors therefore assumed the incidence of BSE in Sweden between 1993 and 2000 to be nil.

Triangular distributions were used to describe the uncertainty of these variables.

Since no data was available to differentiate between the proportion of infective animals among those intended for exportation, those that produce exported meat and those that produce exported MBM, a separate evaluation of the three proportions was impossible and the authors assumed that there is no difference between these categories.

### Table III

<table>
<thead>
<tr>
<th>Country</th>
<th>Expected value for (per million)</th>
<th>Probability distribution for the peak year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denmark</td>
<td>13.2</td>
<td>16.9</td>
</tr>
<tr>
<td>Germany</td>
<td>19.9</td>
<td>25.6</td>
</tr>
<tr>
<td>France</td>
<td>83.7</td>
<td>93.0</td>
</tr>
<tr>
<td>Italy</td>
<td>20.2</td>
<td>23.1</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>27.3</td>
<td>30.8</td>
</tr>
<tr>
<td>Sweden</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Pmn*: bovine spongiform encephalopathy prevalence in country m in year n

[34] Rev. sci. tech. Off. int. Epiz., 22 (3)
Since there is a close temporal association between the detection of infection and pathological changes in the central nervous system (37), the authors assumed that animals that are incubating the disease but have an infective load of the BSE agent too low to be positive to testing are devoid of infectivity, and that the true incidence, estimated as above, represents the proportion of infective animals.

**Probability that an imported animal is sent to an abattoir in Japan in the year \( n \) (\( AB_n \))**

No incineration or burial of imported animals was practised until October 2001 in Japan unless the animals were infected with an infectious disease and destroyed at a Livestock Hygiene Service Center. In 1999, 1,356,649 cattle were slaughtered in slaughterhouses for human consumption (18). The number of fallen stock in that year was estimated by the Animal Health Division of the MAFF to be 156,639 (26). The authors therefore estimated the probability of an animal being sent to an abattoir in Japan, by dividing the number of cattle slaughtered for human consumption by the aggregate of the number of cattle slaughtered and the number of fallen stock (\( 1,356,649 + [1,356,649 + 156,639] = 0.896 \)).

**Probability that an animal is sent to a rendering plant in Japan in the year \( n \) (\( RE_n \))**

According to the MAFF, 88% of fallen stock is sent to a rendering plant, the remainder either being incinerated at a prefecture Livestock Hygiene Service Center or buried (26). The authors therefore estimated the probability of an animal being sent to a rendering plant in Japan, by multiplying the number of fallen stock by 0.88 and dividing the value obtained by the aggregate of the number of cattle slaughtered and the number of fallen stock (\( 156,639 \times 0.88 + [1,356,649 + 156,639] = 0.102 \)).

**Probability that specified risk material is removed from an animal in the year \( n \) in Japan (\( SRM_n \))**

The authors assumed the probability that SRM is removed from an animal in Japan to be zero, as this was not practised in the country until October 2001.

**Removal efficiency of specified risk materials (COS)**

Prior to implementation of EC Regulation No. 270/2002 in 2002, vertebral columns containing dorsal root ganglia, which represent 3.8% of the total infective load of a BSE-affected animal (7), had never been designated as SRM and supposedly, had never been removed in any EU Member State other than the UK, even when the SRM ban was in force (5). The authors therefore assumed that between 1992 and 2000, the efficiency of SRM removal in the EU Member States other than the UK was 96.2% (100% less 3.8%).

Probability that an animal is rendered at 133°C for 20 min. at 3 bar in Japan (\( R_n \))

According to the results of a survey conducted by the MAFF (2), the amount of MBM produced per annum is estimated to be 400,000 MT, of which 21,600 MT to 54,000 MT was subjected to heat-treatment at 133°C for 20 min. at 3 bar (5.4% to 13.4% of the total amount of MBM produced annually in Japan).

Probability that the bovine spongiform encephalopathy agent is inactivated by heating at 133°C for 20 min. at 3 bar (\( COR \))

Riedinger proposes a reduction factor of \( 10^4 \) to \( 10^6 \) following heat-treatment at 133°C for 20 min. at 3 bar (35), but in experiments using scrapie prions, Taylor et al. showed that the BSE agent is only inactivated by at least \( 10^8 \) fold (36). To be on the safe side, treatment by heating at 133°C for 20 min. at 3 bar was assumed to inactivate the BSE agent \( 10^9 \) fold.

**Average amount of meat-and-bone meal produced from one animal (\( W_{mbm} \))**

According to the results of a survey conducted by the MAFF (2), the amount of MBM produced per annum is estimated to be 400,000 MT, of which 21,600 MT to 54,000 MT was subjected to heat-treatment at 133°C for 20 min. at 3 bar (5.4% to 13.4% of the total amount of MBM produced annually in Japan).

**Average amount of bone-in meat produced from one animal (\( W_{meat} \))**

The average weight of a bovine carcass in the 15 EU Member States from 1993 to 2000 was estimated using normal distribution based on data published by the EC (6, 15).

**Average amount of meat-and-bone meal produced from bone-in meat from one animal (\( W_{mbm}^* \))**

Assuming that bone-in meat generates trimmings and scraps composed of fat and bones (and no other organs) and that the returns of fat and bones for MBM are 4% and 45% respectively (8), the average amount of MBM produced from the bone-in meat of one animal was calculated as (65 kg of fat) \( \times 0.04 + (45 \text{ kg of bones}) \times 0.45 = 22.9 \text{ kg} \).

**Probability of generating scraps or trimmings that are rendered into meat-and-bone meal in Japan in the year \( n \) (\( SCR_n \))**

As there is no data available for this probability, bone-in meat imported as half and quarter carcasses was assumed to generate...
scraps or trimmings that are rendered into MBM. The probability was estimated by dividing the amount of half and quarter carcasses by the total amount of bone-in meat imported in the study years (1), and assumed to follow a normal distribution.

**Probability that specified risk material is removed from an animal in producing bone-in meat in the country of origin \( m \) in the year \( n \) \((SME\text{\textsubscript{mn}})\)**

Between 1993 and 2000, animal quarantine authorities in Japan sampled 1,322 consignments from which SRM had supposedly been removed and found 45 consignments contaminated with this material. Based on this result, the authors used a beta distribution as the input variable for this probability.

**Probability that specified risk material is removed from an animal when producing meat-and-bone meal in the country of origin \( m \) in the year \( n \) \((SMB\text{\textsubscript{mn}})\)**

No requirements on the removal of SRM applied to the MBM exported from EU Member States to Japan. However, information on the introduction of SRM removal published in the Opinion of the EC-SSC on the GBR of the respective countries (9, 10, 11, 12, 13, 14) was used to estimate this probability.

In Denmark, no SRM ban was imposed until March 2000, therefore SRM was assumed not to have been removed from the animals when producing MBM in Denmark until March 2000.

In the Netherlands, the SRM ban was not properly implemented until the end of 1998. Therefore, SRM was assumed not to have been removed until the end of 1998, but removed in 1999 and 2000.

In France, a SRM ban was first introduced in April 1996, but implementation of the ban posed problems and in July 1998, enforcement was found to be irregular (10). The authors therefore assumed that SRM was removed from animals producing MBM only after 1999.

In Italy, no SRM ban was implemented except for cattle imported from countries with an incidence of BSE between 1993 and 2000. In Germany, SRM was removed only from cattle imported from countries where a SRM ban was in place on a voluntary basis. Therefore, SRM was assumed not to have been removed from animals producing MBM in Italy and Germany between 1993 and 2000.

For all the countries, the authors assumed that the SRM ban, when implemented, was 90% to 99.9% effective and most likely 99%.

**Probability that an animal is rendered at 133°C for 20 min. at 3 bar when producing meat-and-bone meal in the country of origin \( m \) in the year \( n \) \((RMB\text{\textsubscript{mn}})\)**

The MAFF of Japan required that MBM imported from EU Member States be subjected to heat-treatment at 133°C for 20 min. at 3 bar (17). However, six out of 202 consignments of MBM exported to Japan from Italy did not comply with this standard. Therefore, the authors considered that although such treatment was required under animal health requirements and compliance with this requirement was confirmed by accompanying health certificates on arrival in Japan, the probability that the MBM in fact underwent this treatment was not 100%. Based on the experience of the imports from Italy, the authors assumed that this probability is 97% at minimum, 99% at maximum and most likely 98%.

Values for these input variables and their probability distributions are shown in Tables I, II, III, IV and V.

### Results

Simulation based on five thousand iterations using the model and input variables described above produced a release risk,

<table>
<thead>
<tr>
<th>Table IV</th>
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</thead>
<tbody>
<tr>
<td><strong>Probability that specified risk material (SRM) is removed from an animal in producing meat-and-bone meal (MBM) in countries in Europe (SMB\text{\textsubscript{mn}}*)</strong></td>
</tr>
<tr>
<td>Denmark</td>
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<tr>
<td>Germany</td>
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<tr>
<td>France</td>
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<tr>
<td>Italy</td>
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<tr>
<td>The Netherlands</td>
</tr>
<tr>
<td>Sweden</td>
</tr>
</tbody>
</table>

* SME\text{\textsubscript{mn}}: probability that SRM is removed from an animal in producing MBM in country of origin \( m \) in year \( n \)
expressed as the weight of infected MBM released in Japan in the past eight years, of 23.4 kg to 53.8 kg with a probability of 95%.

Table VI and Figure 4 show the amount of MBM released in Japan under different scenarios. Apparently, importation of MBM resulted in the highest release risk factor, while importation of live cattle and bone-in carcass meat appears to constitute a lesser risk of release.

Discussions and conclusion

Cases of bovine spongiform encephalopathy detected in Japan

Five cases of BSE have been detected in Japan at the time of writing this paper. The first case was detected on 10 September 2001, from a brain sample of a five-year old dairy cow with ataxia slaughtered on 6 August 2001 at an abattoir in the Chiba-prefecture, east of Tokyo. The other four cases, without clinical signs, were also dairy cows found to be infected as the result of BSE testing using prion protein technology conducted at abattoirs. The details and geographical locations of these five cases are shown in Table VII and Figure 5, respectively.

The MAFF had taken various preventive measures even before the first case of BSE was detected in Japan in September 2001. These consisted of an import ban on live cattle from countries with a high incidence of BSE, SRM removal from meat products from countries with an incidence of BSE, importation of MBM subjected to heat treatment at 133°C for 20 min. at 3 bar, administrative instructions to control the use of ruminant MBM for ruminant feed, etc. These measures proved to be insufficient to protect Japan from being affected by BSE. The results of the BSE release assessment show that between 23.4 kg and 53.8 kg of infected MBM (equivalent to 0.49-1.12 infected animals), originating mostly from imported MBM, may possibly have been released in Japan from 1993 to 2000.

Table V

<table>
<thead>
<tr>
<th>Input variables</th>
<th>Values for 1993-2000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Expected value</td>
</tr>
<tr>
<td>Probability that an animal is sent to an abattoir in Japan in year n (ABn)</td>
<td>89.6%</td>
</tr>
<tr>
<td>Probability that an animal is sent to a rendering plant in Japan in year n (REn)</td>
<td>10.2%</td>
</tr>
<tr>
<td>Probability that SRM is removed from an animal in Japan (Sn)</td>
<td>0.0%</td>
</tr>
<tr>
<td>Efficiency of SRM removal (CDS)</td>
<td>0.962</td>
</tr>
<tr>
<td>Probability that an animal is rendered at 133°C/20 min./3 bar in Japan (Rn)</td>
<td>9.4%</td>
</tr>
<tr>
<td>Probability that the BSE agent is inactivated by treating at 133°C/20 min./3 bar (COR)</td>
<td>0.998</td>
</tr>
<tr>
<td>Average weight of MBM produced from one animal (Wmbm) (kg)</td>
<td>48.0</td>
</tr>
<tr>
<td>Average weight of bone-in meat produced from one animal (Wmeat) (kg)</td>
<td>275.3</td>
</tr>
<tr>
<td>Average weight of MBM produced from bone-in meat from one animal (Wmbm'') (kg)</td>
<td>22.9</td>
</tr>
<tr>
<td>Probability that SRM is removed from an animal in producing bone-in meat in the country of origin m in the year n (SMEmn)</td>
<td>96.5%</td>
</tr>
<tr>
<td>Probability that an animal is treated at 133°C/20 min./3 bar for the production of MBM in the country of origin m in the year n (RMBmn)</td>
<td>98.0%</td>
</tr>
</tbody>
</table>

MBM: meat-and-bone meal
SRM: specified risk material

Table VI

<table>
<thead>
<tr>
<th>Scenario</th>
<th>2.5% percentile</th>
<th>5% percentile</th>
<th>50% percentile</th>
<th>95% percentile</th>
<th>97.5% percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total amount of infected MBM released between 1993 and 2000 (RRtotal) (kg)</td>
<td>23.400</td>
<td>25.000</td>
<td>36.300</td>
<td>50.600</td>
<td>53.800</td>
</tr>
<tr>
<td>Amount of infected MBM released following importation of live cattle (RRanimal) (kg)</td>
<td>0.008</td>
<td>0.009</td>
<td>0.014</td>
<td>0.018</td>
<td>0.019</td>
</tr>
<tr>
<td>Amount of infected MBM released following importation of bone-in meat (RRmeat) (kg)</td>
<td>0.036</td>
<td>0.036</td>
<td>0.051</td>
<td>0.066</td>
<td>0.069</td>
</tr>
<tr>
<td>Amount of infected MBM released following importation of MBM (RRmbm) (kg)</td>
<td>23.300</td>
<td>24.900</td>
<td>36.200</td>
<td>50.500</td>
<td>53.700</td>
</tr>
</tbody>
</table>
Fig. 4
Probability distribution of the amount of infected meat-and-bone meal released in Japan between 1993 and 2000 through different scenarios

RR: release risk
MBM: meat-and-bone-meal
If an infected animal is equivalent to 8,000 oral cattle infectivity doses (ID50) (as assumed by the EC-SSC [7]), the infected MBM possibly released in Japan between 1993 and 2000 was equivalent to 3,920 ID50-8,967 ID50 (this would have infected a maximum of 3,920-8,967 animals if there were no exposure control and the infected MBM was evenly distributed to this number of cattle). The exposure assessment remains to be completed to estimate the possible number of cattle infected during this period.

Exposure assessment

Before the first case of BSE was detected in September 2001, the MAFF presumed that controls on the use of ruminant MBM in ruminant feed were effectively enforced according to administrative instructions issued by the Ministry on 17 April 1996. This presumption was supported by the fact that no breach of instructions had been observed during on-the-spot inspections of feed mills by the National Fertilizer and Feed Inspection Stations (NFFIS). During these inspections, inspectors from the NFFIS checked production records and sampled cattle feed for microscopic examination to ensure that the MBM in ruminant feed was not contaminated.

Regarding the possibility of cross-contamination and cross-feeding at farm level between cattle, pig and chicken feed, the MAFF was of the view then that there is little chance that this would occur in Japan for three reasons, as follows:

– co-farming of ruminants and non-ruminants is not a common practice in Japan. In February 2000, of the 33,328 dairy farms and 106,101 beef cattle farms in Japan, 116 dairy farms (0.03%) and 847 beef farms (0.8%) also had non-ruminant animals (20)

– there is no economic advantage in using MBM for cattle feed as a substitute for plant protein supplements as the price difference between animal protein (including MBM) and vegetable protein (soya) is negligible

– in Japan, farmers do not usually keep MBM on their premises and prepare home-mixed feed.

In addition, before the administrative instruction was issued on 17 April 1996, the MAFF had considered that the quantities of MBM fed to cattle was negligible: the amount used before that date as raw material for the production of cattle compound feed was 99 MT to 247 MT annually, representing less than 0.05% of the total amount of MBM used for feed (Table VIII).

However, on-site inspections of all cattle farms in Japan by prefecture veterinary inspectors in September 2001 after detection of the first case of BSE revealed that 165 cattle farms in fifteen prefectures were feeding some processed animal proteins (mainly MBM, blood meal or steamed bone meal) to a total of 5,129 cattle (22, 23). These animal proteins were fed as supplements, mainly on dairy farms. At the time of writing this
paper, none of these farms had experienced a case of BSE. Considering the sensitivity of the microscopic examinations and the fact that some feed mills were found to produce ruminant and non-ruminant feed on the same production line, the possibility of cross-contamination cannot be excluded. To complete the exposure assessment, additional information should be obtained on the feeding histories of animals on these farms as well as details on cross-contamination and cross-feeding between 1993 and 2000.

**Possible sources of infection**

Immediately after the first case of BSE was detected in September 2001, the MAFF organised an investigation team to identify the source of infection, assuming that the agent was introduced into Japan and exposed to the infected cows between 1996 and early 1998. Considering the fact that the five infected cows were all born between December 1995 and April 1996 and that susceptibility in cattle peaks between 0.5 to 1.5 years of age (39), the MAFF assumed that these cows had been most susceptible in 1996 and 1997. The MAFF has concluded in an interim report that the following two possibilities cannot be ruled out with regard to the five cases:

– contamination with MBM, possibly by feed cross-contaminated in feed mills with MBM imported from Italy in November 1996, which had not been heat-treated at 133°C/20 min./3 bar

– use of contaminated animal fat (powdered animal fat imported from the Netherlands between 1995 and May 1996) in feed for cattle and in milk replacers for calves.

In addition to the possibilities mentioned above, the fact that the BSE agent may have entered Japan through cattle imported from the UK in the 1980s, from Germany in 1993, from MBM imported from countries in Europe before 1995 and that the source of infection may have been MBM from Japan could not be completely excluded, and more information on this subject needs to be collected in future. Judging from the geographical locations of the five cases detected, more than one batch of MBM was assumed to be contaminated with the BSE agent. Although adult exposure is a possibility (38), MBM imported from Europe between 1999 and 2000 is unlikely to have been the source of infection. If this were the case, the incubation periods would have been shorter than 33-61 months, which was the period determined by experimental exposure of four-month old calves to one or three doses of 100 g of infective bovine brain by the oral route (D. Matthews, Veterinary Laboratories Agency, 2002, personal communication).

The experience in countries in Europe shows that these investigations rarely result in successful identification of the source of infection. In addition to addressing the specifics of the BSE cases detected to date, further investigations and assessment of the risk factors that might have played a role in introducing and propagating the disease should be conducted. This would allow identification of the measures to be taken to prevent the BSE agent from entering into the feed chain, even in the absence of any clear link to imported products.

**Animal health and public health measures taken in Japan**

The measures taken to protect animal and public health from BSE in Japan are shown in chronological order in Table IX. Following detection of the first case of BSE, the Government of Japan, mainly the MAFF and the Ministry of Health, Labor and Welfare (MHLW), introduced the measures described below to prevent the agent from entering into the feed chain:

- Active surveillance was initiated on 18 October 2001 (BSE testing of 4,500 cattle annually, randomly sampled from fallen stock. This will be intensified so that all fallen stock over
24 months of age will be tested for BSE from April 2003, except for remote islands and geographically vast areas. The results of this surveillance as of 4 October 2002 and the number of animals subjected to laboratory tests before 20 December 2002 are shown in Table X [24, 28].

b) BSE testing of all cattle slaughtered for human consumption was initiated on 18 October 2001 using enzyme-linked immunosorbent assay (ELISA) kits. By 30 November 2002, 1,327,230 cattle had been tested with four positive cases being detected as shown in Table XI (32).

c) Removal of SRM (brains, spinal cord, eyes and distal ileum) from all cattle slaughtered for human consumption was initiated on 27 September 2001 and implemented under the Abattoir Law Enforcement Regulation amended on 18 October 2001 (31). Removed SRM is incinerated directly at the slaughterhouses.

d) The MHLW recommended that domestic food industries use materials that do not contain SRM originating from countries with an incidence of BSE and that all products containing SRM be recalled (30).

e) A legal ban on the domestic use of ruminant protein for ruminant feed was implemented on 18 September 2001 (25), followed by a ban on the domestic use and import of all processed animal proteins for the production of feed for ruminants, pigs and chickens and fertiliser, effective from 4 October 2001. To ensure compliance and to prevent cross-contamination, the MAFF has instructed feed mills to apply flushing or to use a different line to produce ruminant feed. The mills are subjected to regular visits by inspectors of the NFFIS, who take samples for microscopic examination and laboratory tests such as the polymerase chain reaction and ELISA tests (domestic use of pig and chicken meal for fertiliser and pet food) 

<table>
<thead>
<tr>
<th>Date</th>
<th>Measures taken</th>
</tr>
</thead>
<tbody>
<tr>
<td>1951</td>
<td>Import of beef prohibited from Great Britain for foot and mouth disease reasons</td>
</tr>
<tr>
<td>July 1990</td>
<td>Import of live cattle prohibited from the United Kingdom (UK) and other countries with an incidence of BSE</td>
</tr>
<tr>
<td></td>
<td>Import of meat-and-bone meal (MBM) prohibited from the UK and other countries with an incidence of BSE except for MBM heat-treated at 133°C/30 min. at 3 bar</td>
</tr>
<tr>
<td>March 1996</td>
<td>Import of MBM from the UK totally prohibited</td>
</tr>
<tr>
<td></td>
<td>Import of beef and by-products prohibited from the UK</td>
</tr>
<tr>
<td>April 1996</td>
<td>Administrative guidance issued to prohibit the use of ruminant MBM for ruminant feed</td>
</tr>
<tr>
<td></td>
<td>BSE designated as a notifiable disease</td>
</tr>
<tr>
<td>January 2001</td>
<td>Import of MBM prohibited from European Union Member States, Switzerland and Liechtenstein</td>
</tr>
<tr>
<td>April 2001</td>
<td>Domestic BSE surveillance strengthened</td>
</tr>
<tr>
<td>September 2001</td>
<td>First case of BSE detected</td>
</tr>
<tr>
<td></td>
<td>Legal prohibition of the use of ruminant MBM for ruminant feed</td>
</tr>
<tr>
<td></td>
<td>Specified risk material removal from all cattle for human consumption</td>
</tr>
<tr>
<td>October 2001</td>
<td>Import of processed animal protein prohibited from all countries</td>
</tr>
<tr>
<td></td>
<td>BSE testing of all cattle for human consumption</td>
</tr>
<tr>
<td></td>
<td>Domestic surveillance strengthened</td>
</tr>
<tr>
<td>December 2001</td>
<td>Import of powdered animal fat prohibited from all countries</td>
</tr>
<tr>
<td>January 2002</td>
<td>Use of ruminant animal fat with an impurity level of over 0.02% for milk replacer prohibited</td>
</tr>
</tbody>
</table>

Table IX
Chronology of bovine spongiform encephalopathy (BSE) measures taken in Japan

<table>
<thead>
<tr>
<th>Date</th>
<th>Measures taken</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>Import of beef prohibited from Great Britain for foot and mouth disease reasons</td>
</tr>
<tr>
<td>1997</td>
<td>Import of live cattle prohibited from the United Kingdom (UK) and other countries with an incidence of BSE</td>
</tr>
<tr>
<td>1998</td>
<td>Import of meat-and-bone meal (MBM) prohibited from the UK and other countries with an incidence of BSE except for MBM heat-treated at 133°C/30 min. at 3 bar</td>
</tr>
<tr>
<td>1999</td>
<td>Import of MBM from the UK totally prohibited</td>
</tr>
<tr>
<td>2000</td>
<td>Import of beef and by-products prohibited from the UK</td>
</tr>
<tr>
<td>2001</td>
<td>Administrative guidance issued to prohibit the use of ruminant MBM for ruminant feed</td>
</tr>
<tr>
<td>2002</td>
<td>BSE designated as a notifiable disease</td>
</tr>
<tr>
<td>2003</td>
<td>Specified risk material removal from all cattle for human consumption</td>
</tr>
</tbody>
</table>

Table X
Results of bovine spongiform encephalopathy surveillance in Japan from 1996 to June 2002

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle over 24 months with clinical signs</td>
<td>23</td>
<td>20</td>
<td>36</td>
<td>36</td>
<td>24</td>
<td>336</td>
<td>254</td>
</tr>
<tr>
<td>Cattle over 24 months without clinical signs</td>
<td>194</td>
<td>203</td>
<td>210</td>
<td>237</td>
<td>227</td>
<td>0</td>
<td>32</td>
</tr>
<tr>
<td>Fallen animals</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>770</td>
<td>1,866</td>
</tr>
<tr>
<td>Total</td>
<td>217</td>
<td>223</td>
<td>246</td>
<td>273</td>
<td>251</td>
<td>1,106</td>
<td>2,152</td>
</tr>
</tbody>
</table>

* as of 20 December 2002
Source: Animal Health Division, Ministry of Agriculture, Forestry and Fisheries, Japan
food, and chicken meal and powdered pig plasma for pig and chicken feed has been allowed since 1 November 2001, and domestic use of steamed bone meal as fertiliser has been allowed under certain conditions) (21).

Animal identification systems have been introduced, which will enable back-tracing to the farm of origin to access other relevant information from the bar code on the ear tag of each individual animal. Almost all of the 4.5 million cattle in Japan had been ear tagged under this system by the end of March 2002 (27).

The Government of Japan introduced these measures in the six months following detection of the first case of BSE, a relatively short time compared to most of the EU Member States. Assuming these measures continue to be appropriately implemented, the probability that cattle are (pre-clinically or clinically) infected with the BSE agent will continue to decrease over time. However, the experience in Europe shows that measures prescribed by law and regulations are not always completely implemented. Early establishment of an effective surveillance network, including active surveillance targeted at risk animals, is essential to monitor the effectiveness of these measures as well as to estimate the possible year when the BSE agent entered Japan.

The release assessment model outlined in this paper is based on the assumption that importation of live cattle, bone-in carcass meat and MBM between 1993 and 2000 are the risk factors. If evidence is found to support the hypothesis that the BSE agent entered Japan more than eight years ago, the model described will have to be reconstructed so as to accommodate the risk relating to domestic sources of the agent. This precaution should also apply when using the model to determine the BSE status of another country. The model can be applied to assess the BSE status of a country only when there is no possibility that the agent entered into the country more than eight years ago. Furthermore, the release assessment model outlined in this paper only considers the importation of live cattle, bone-in carcass meat and MBM as risk factors. If any release risk factors other than these, such as imported animal fat, proved to be important, the model will have to be reconstructed to take account of these risk factors as well.

Acknowledgement

The authors would like to thank Dr R. Bradley, BSE Consultant in the UK, Mr D. Vose, Risk Consultant in France and Dr N. Murray, Risk Analysis Group, Animal Biosecurity, Ministry of Agriculture and Forestry of New Zealand, for their useful suggestions and comments.

Table XI
Results of bovine spongiform encephalopathy testing at slaughterhouses from 18 October 2001 to 30 November 2002

<table>
<thead>
<tr>
<th>Date of sampling</th>
<th>Animals with clinical signs*</th>
<th>Healthy animals over 30 months of age</th>
<th>Other healthy animals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of animals tested</td>
<td>Animals with positive results</td>
<td>Number of animals tested</td>
</tr>
<tr>
<td>18-31 October 2001</td>
<td>339</td>
<td>0</td>
<td>10,955</td>
</tr>
<tr>
<td>1-30 November 2001</td>
<td>466</td>
<td>0</td>
<td>43,515</td>
</tr>
<tr>
<td>1-31 December 2001</td>
<td>190</td>
<td>0</td>
<td>38,630</td>
</tr>
<tr>
<td>1-31 January 2002</td>
<td>217</td>
<td>0</td>
<td>36,969</td>
</tr>
<tr>
<td>1-28 February 2002</td>
<td>196</td>
<td>0</td>
<td>38,333</td>
</tr>
<tr>
<td>1-31 March 2002</td>
<td>443</td>
<td>0</td>
<td>47,230</td>
</tr>
<tr>
<td>1-30 April 2002</td>
<td>234</td>
<td>0</td>
<td>51,650</td>
</tr>
<tr>
<td>1-31 May 2002</td>
<td>221</td>
<td>1</td>
<td>46,205</td>
</tr>
<tr>
<td>1-30 June 2002</td>
<td>170</td>
<td>0</td>
<td>38,299</td>
</tr>
<tr>
<td>1-31 July 2002</td>
<td>252</td>
<td>0</td>
<td>47,645</td>
</tr>
<tr>
<td>1-31 August 2002</td>
<td>247</td>
<td>1</td>
<td>40,843</td>
</tr>
<tr>
<td>1-30 September 2002</td>
<td>233</td>
<td>0</td>
<td>39,355</td>
</tr>
<tr>
<td>1-31 October 2002</td>
<td>237</td>
<td>0</td>
<td>45,873</td>
</tr>
<tr>
<td>1-30 November 2002</td>
<td>124</td>
<td>0</td>
<td>24,607</td>
</tr>
<tr>
<td>Total</td>
<td>3,567</td>
<td>2</td>
<td>500,071</td>
</tr>
</tbody>
</table>

* animals over twenty-four months of age showing clinical signs such as locomotive inco-ordination, sensory disorders, or reflex disorders at the time of ante-mortem inspection

Source: Ministry of Health, Labor and Welfare, Japan
Modèle d’évaluation du risque d’introduction de l’agent de l’encéphalopathie spongiforme bovine au Japon par le biais des importations d’animaux, de viandes et de farine de viande et d’os

K. Sugiura, K. Ito, R. Yokoyama, S. Kumagai & T. Onodera

Résumé

Mots-clés

Moderno para determinar el riesgo de introducción en Japón del agente de la encefalopatía espongiforme bovina a través de animales, carne y harinas de carne y huesos de importación

K. Sugiura, K. Ito, R. Yokoyama, S. Kumagai & T. Onodera

Resumen
Los autores elaboraron un modelo matemático para determinar el riesgo de liberación en un país del agente de la encefalopatía espongiforme bovina (EEB) a resultas de la importación de ganado vivo, carne bovina no desosada o harinas de carne y huesos procedentes del Reino Unido o de algún otro país afectado por la enfermedad. Utilizando ese modelo e incorporándole una serie de variables se intentó aplicar la simulación de Montecarlo. Se estimó que el riesgo de penetración del agente en Japón, expresado como el peso de harinas infectadas que entraron en el país entre 1993 y 2000, se situaba entre 23,4 y 53,8 kg. La simulación puso también de manifiesto que las harinas importadas constituían el
principal factor de riesgo de penetración del agente de la EBB en Japón. Los autores ofrecen también información sobre los cinco primeros casos de EEB detectados en Japón entre septiembre de 2001 y finales de 2002, y exponen a grandes líneas los resultados de la investigación para determinar el origen de la infección, así como las medidas adoptadas por el Gobierno japonés para impedir que el agente infeccioso penetra en la cadena alimentaria y en el circuito de producción de piensos.

**Palabras clave**

**References**


8. European Commission (EC) (1999). – Scientific Report on the risks of non conventional transmissible agents, conventional infectious agents or other hazards such as toxic substances entering the human food or animal feed chains via raw material from fallen stock and dead animals (including also: ruminants, pigs, poultry, fish, wild/exotic/zoo animals, fur animals, cats, laboratory animals and fish) or via condemned materials. EC, Brussels, 70 pp.


34. OIE (World organisation for animal health) (2002). – Annual incidence rate of bovine spongiform encephalopathy (BSE) in countries that have reported cases, excluding the United Kingdom, OIE, Paris, 2 pp. (http://www.oie.int/eng/info/en_esbincidence.htm accessed on 5 December 2002).


