BOVINE SPONGIFORM ENCEPHALOPATHY AS AN EMERGING DISEASE: MEASURES, WAYS AND MEANS TO PROTECT ANIMALS AND CONSEQUENTLY HUMANS FROM THE POSSIBLE RISK OF DISEASE

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Summary: Reports were received from eight Member Countries: Cyprus, Jordan, Kuwait, Oman, Qatar, Saudi Arabia, Turkey and United Arab Emirates.

Information from these countries indicated that all have substantial numbers of ruminant food animals known to be naturally susceptible to transmissible spongiform encephalopathy (TSE), namely bovine spongiform encephalopathy (BSE) or scrapie. Only one country reported mink farming on a small scale but most countries have at least one zoo housing Bovidae and Felidae. Only one country reported cases of scrapie in sheep and goats. However, in this country a continuous and comprehensive control programme has existed since 1987.

Most countries have imported live ruminant animals and ruminant bone-in carcass meat, sometimes on a large scale. Few countries have imported meat and bone meal (MBM).

In six countries BSE and scrapie are notifiable diseases and seven have awareness programmes in place. Five countries have facilities for post mortem confirmation of TSE by microscopic examination of the brain but by no other method. Training has been provided by Germany, the United Kingdom (UK) and the United States of America for three countries. The three other countries would consult a reference centre in another country if necessary.

Two countries prohibited the feeding of mammalian protein to ruminant animals. Two countries have some form of specified bovine offals ban for animal and/or human consumption.

Two countries reported the use of animal/ruminant waste rendering with conditions equivalent to, or in excess of, those in use in the European Union (EU) and proposed by the OIE. One country exports waste after initial treatment. The other countries incinerate or bury such waste.

Dead animals are incinerated or buried in all countries.

No country has conducted a risk assessment for BSE or scrapie and no risk management strategy has been adopted. No data were presented on monitoring or surveillance for BSE or scrapie.

Three countries use the recommendations in the OIE International Animal Health Code regarding the importation of cattle and cattle products. Two do not import these materials from countries that have had confirmed cases of BSE.

Creutzfeldt-Jakob disease (CJD) is notifiable in four countries and two have a surveillance programme. One country reported one case and another country reported two cases of conventional sporadic CJD during the period 1990-1996. No cases of the new variant CJD (vCJD) were reported in any country.

In Europe BSE occurs in native-born cattle in six countries. Both in the UK and Switzerland the incidence is declining in response to control measures. In the UK (21 cases) and in France one case of vCJD has occurred. To date there is no direct evidence that BSE causes vCJD but the possibility that it could remains.

Control measures in regard to animal feed, rendering and specified risk materials are in place or proposed in all Member States of the EU.
All countries should conform with the recommendations of the OIE International Animal Health Code chapter on BSE (3.2.13) and especially conduct a risk assessment for BSE and adopt a risk management strategy to reduce any risk identified.

These procedures will reduce any risk there may be for animals and humans and will assist in the eradication of BSE from OIE Member countries.

1. INTRODUCTION

1.1. Bovine spongiform encephalopathy and related diseases

Bovine spongiform encephalopathy (BSE) is a newly recognised transmissible spongiform encephalopathy (TSE) of adult cattle (41), the first clinical case occurring in Great Britain (GB) in April 1985. Cases in native-born cattle are restricted to the United Kingdom (UK), France, Portugal, the Republic of Ireland, The Netherlands and Switzerland (27). The incidence was much higher in the UK than in the other countries with BSE but is now declining rapidly as a result of effective control measures largely related to preventing new infections in feed (26). The incidence is also declining in Switzerland (27) and France (E. Bonbon, personal communication). By contrast, the incidence is increasing in the other listed countries though the annually reported cases are few.

BSE is a member of the group of diseases known as the sub-acute, transmissible spongiform encephalopathies (TSE) or prion diseases (3). These include Creutzfeldt-Jakob disease (CJD) of man, scrapie of sheep and goats, transmissible mink encephalopathy (TME) and, in North America only, chronic wasting disease (CWD) of wapiti (Cervus canadensis) and some deer species. These diseases can only certainly be confirmed post mortem by examination of the brain. The agents causing these diseases are not clearly defined (they may be prions, virions or unconventional viruses) (32). They provoke no immune response in the host (consequently there is no practical and effective test to detect infected animals) and are exceedingly resistant to inactivation by heat radiation or chemicals (37). All the diseases are invariably fatal. The highest titres of infectivity, measured by bioassay, are found in the central nervous system (CNS) of advanced clinical cases. Infectivity is, or may be, present in the lymphoreticular tissues and/or the CNS during the incubating phase of the disease but is not detectable until some months after exposure. In cattle with clinical BSE, infectivity has been found only in the brain, spinal cord and retina of the eye (19, 25). Infectivity has never been found in milk or meat in natural cases of any animal TSE. Control measures can therefore reduce the risk of exposure occurring in any species (including man) by concentrating the effort on eliminating animals clinically suspected to have BSE from all food and feed chains and destroying the specified risk materials (i.e. those most likely to contain infectivity, especially CNS tissues) from all cattle over a specified age whether killed for human consumption or not.

1.2. Feed origin of infection

There is no doubt that BSE (and the related diseases in domestic cats and captive wild animals) are feed-borne diseases. In cattle and captive wild Bovidae the vehicle is meat and bone meal (MBM) (46, 47) containing ruminant protein derived from infected offals (specified risk materials) the most important of which are CNS tissues. The original species source for BSE could have been cattle but it is more plausible that sheep with scrapie were responsible since this is the only known animal reservoir of TSE infection (43). Whatever the source, the epidemic was subsequently fuelled by the recycling of infected cattle tissues via feed (42). Feed-borne exposure to BSE or scrapie agents may also have caused cases of scrapie in sheep and/or goats though there is no direct evidence that this has occurred in practice. If the BSE agent has infected sheep and/or goats it could pose a risk for man. Some countries have taken steps to prevent this by imposing some form of ovine and caprine offals ban as part of a risk-reduction strategy. These bans concentrate on the CNS and prohibit consumption by man and animals.

1.3. Maternal transmission

Recent data from a cohort study (36) suggest that despite the average risk of maternal transmission of BSE to calves being just under 1% neither maternal nor horizontal transmission can maintain the UK epidemic as the
minimum necessary 1 to 1 contact rate cannot be maintained (42). The key feature of control therefore is by eliminating feed-borne exposure (45). The risk of maternal transmission is greatest for calves born after the date of onset of BSE in the dam. For calves born before the onset of BSE in the dam the risk was lower and further reduced as the interval between birth and disease onset increased. There was no increased risk when this interval was two years or more. The mechanism of transmission is not known but a combination of increased genetic susceptibility to infection in feed and agent transmission best fit the data (36).

1.4. Creutzfeldt-Jakob disease

CJD is a rare disease (one case per 1-2 million pa world-wide). About 85% of cases are sporadic and the cause is not known (22). Most of the remainder are familial and related to mutations in the PrP gene. Familial CJD is both hereditary and infectious. A small number of iatrogenic cases of CJD due to historical medical accidents have transmitted disease from one human to another. There is no direct evidence to date that any animal TSE has transmitted naturally to man or vice versa.

From October 1995 onwards, a small number of cases of a new variant form of CJD (nvCJD or vCJD) has been reported (48). Ten cases were reported in the UK on 20 March 1996 by the Secretary of State for Health. The total number of cases to 31 July 1997 is 21 cases in the UK and one in France. There is no direct evidence that BSE is the cause of these cases. There is no obvious connection with occupation or with feeding habits. All cases examined to date are homozygous for methionine at codon 129 of the PrP gene. The temporal and geographical occurrence of vCJD suggests, in the absence of any other obvious cause, that exposure to BSE before measures were taken to protect public health (i.e. before 1988/89) could have been responsible (35). Consequently further steps to strengthen the statutory control and to enforce and ensure complete compliance in regard to bovine products, particularly specified risk materials, have been taken (25). The results of unannounced abattoir visits and assays of animal feeds are published regularly in BSE Enforcement Bulletins and Meat Hygiene Enforcement Reports so the public can see how effectively the controls have been applied. Since March 1996 the use of mammalian MBM in any feed for food animals, horses or fish has been banned (25). Also, in addition to existing controls, but with certain rare exceptions concerning grass-fed cattle up to 42 months of age in an officially controlled beef assurance scheme, meat or meat products only from cattle under 30 months old are permitted for sale. Cattle older than this are destroyed at the end of their productive life.

1.5. Action by the European Commission

Because of the free-trading situation in the European Union, the need for consistency and to protect animal and public health the European Commission (EC) has imposed various conditions on all Member States including prohibition of the feeding of mammalian MBM to ruminant animals (13) and specifications for the rendering of ruminant materials (15). Importantly to re-establish consumer confidence in beef, the export of live cattle, meat and meat products from the UK has been temporarily prohibited (14). There are no restrictions on the export of milk and semen. The most recent restriction is a Union-wide specified risk materials* ban effective from 1 January 1998 (16). This will include CNS tissues from cattle, sheep and goats over one year old and the spleen of sheep and goats of any age.

1.6. Connection between bovine spongiform encephalopathy and new variant Creutzfeldt-Jakob disease

Whether or not BSE causes vCJD is under intense investigation using strain typing (5, 6), transgenic mice (9), molecular analyses of PrP (10, 29, 34), in vitro, cell free assays for the conversion of PrPSc into PrPSc using PrPSc from a different species (30) and epidemiological techniques (48). At present uncertainty remains.

1.7. Scrapie control

Some countries including the UK, Norway, Iceland, Cyprus and the United States of America (USA) have scrapie-control schemes in place. The recent research results from several countries relating to the association of particular polymorphisms in the PrP gene with scrapie occurrence or resistance (21) are now being applied, notably in the UK (2, M. Dawson, personal communication), so that a scrapie-resistant population can be built up. In contrast to BSE, scrapie is contagious and this is why it is maintained as an endemic disease in most countries in which it occurs. The role of the scrapie-resistant carrier sheep has yet to be elucidated, if indeed it exists.

1.8. Other bovine spongiform encephalopathy research

* Specified risk material: skull, including the brain, eyes, tonsils and spinal cord from bovine, ovine and caprine animals over 12 months old and the spleens of ovine and caprine animals.
Much research is in progress to develop a marker test for infection e.g. using lymphoreticular tissue (to detect PrPSc, 33), cerebrospinal fluid (23) and urine (R. Jackman, personal communication) at an early stage of incubation, to establish sound inactivating procedures (including via rendering) and to develop quick methods for strain typing isolates in order to aid epidemiological tracing.

1.9. Protection against bovine spongiform encephalopathy

The key features needed to protect cattle and other species from BSE are:

- Awareness of veterinarians and farmers of the clinical signs.
- Compulsory notification and clinical investigation of suspect cases.
- Laboratory examination of brains as specified in the OIE Manual.
- A risk assessment comprising assessment of:
  i) **exogenous risks** from imported live animals, embryos or ova or from imported, compounded feed concentrate or meat and bone meal, and
  ii) **endogenous risks** from contaminated feed, from inadequate rendering procedures or from maternal transmission from imported animals.
- A continuous BSE surveillance and monitoring system.
- Maintenance of records for at least seven years.

Protection against BSE in Middle East countries can be provided by implementation of the OIE *International Animal Health Code* chapter on BSE (28).

1.10. Animal and public health protection

For discussion purposes the protection of animal health and public health can be conveniently separated (39). It is important to recognise that elimination of BSE from cattle would be expected to reduce any risk of exposure to man to a very low level indeed. There are two provisos. First, that BSE infectivity does not exist in any other food animal species. Secondly that if BSE ‘the disease’ is eliminated, infectivity at the level necessary to transmit disease to any other species is eliminated also. In regard to the first point, of the food animal species other than cattle, only sheep and goats have succumbed to oral challenge with BSE infectivity (18) but there is no evidence that this has naturally occurred in the UK or anywhere else.

1.11. Control measures

Effective measures to protect animal and public health from BSE depend upon the following features.

In all countries:
- An ability to identify clinically affected animals.
- Compulsory notification and clinical investigation of suspect cases which are compulsorily slaughtered.
- Confirmation of disease *post mortem* by a method specified in the OIE Manual.
- Complete destruction of confirmed cases so they can enter no feed or food chain.

In countries with BSE in native-born cattle:
- The introduction and enforcement of a ruminant feed ban.
- Removal from all food and feed chains of brain, eyes, spinal cord and distal ileum from cattle over six months of age and born before the date on which the ruminant feed ban was effectively enforced.
- The introduction of an approved rendering process for waste ruminant material.

In all countries:
- The introduction of a sound risk management strategy developed from a risk assessment of exogenous and endogenous risks for BSE.
- The continuous surveillance and monitoring for BSE which must include examination in an approved laboratory of a statistically valid number of brains from targeted cattle over 20 months old showing progressive neurological disease.
2. SUMMARY OF REPORTS

The cattle, sheep and goat, pig, poultry and human populations in thousands are given for each country in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Cattle</th>
<th>Buffalo</th>
<th>Sheep</th>
<th>Goats</th>
<th>Pigs</th>
<th>Poultry</th>
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<td>72</td>
<td>NFP</td>
<td>280</td>
<td>275</td>
<td>400</td>
<td>16,420</td>
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<tr>
<td>Jordan</td>
<td>76</td>
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<td>-</td>
<td>NFP</td>
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<td>NFP</td>
<td>267</td>
<td>886</td>
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<td>199</td>
<td>172</td>
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<td>0</td>
<td>300,000</td>
</tr>
<tr>
<td>Turkey</td>
<td>11,866</td>
<td>235</td>
<td>33,072</td>
<td>9,482</td>
<td>5</td>
<td>138,737</td>
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<tr>
<td>United Arab Emirates</td>
<td>69</td>
<td>-</td>
<td>356</td>
<td>920</td>
<td>-</td>
<td>20,000</td>
</tr>
</tbody>
</table>

NFP: No figure provided
- : Believed to be zero

2.1. Cyprus

The Department of Veterinary Services has overall responsibility and authority in regard to animal and public health aspects concerning zoonosis control, meat, milk and milk product hygiene via five District Veterinary Offices and 12 subsidiary Rural Veterinary Stations.

There is one zoo housing species of Bovidae, Cervidae and Felidae and this is under State Veterinary control. No mink are farmed. TSE have not been identified in any of the captive species. Carcases of dead animals are incinerated or buried.

BSE has never been diagnosed in Cyprus. Scrapie has been confirmed in 1106 native-born sheep since 1985. The last case was diagnosed in 1997. A continuous comprehensive control programme was initiated in 1987 involving twice yearly inspections of animals, movement and breeding records. Scrapie-affected animals and others are compulsorily slaughtered and compensation is paid. Brains are examined and premises disinfected. Exogenous risk factors in regard to BSE and scrapie exist due to importation. Precautions are taken according to OIE recommendations in order to reduce risk. However, recent imports from Greece (a low risk country for scrapie) have been restricted to 22 sheep in 1991, five goats in 1989 and 26 in 1991.

Large quantities (thousands of tonnes) of deboned and bone-in beef and lamb have been imported annually in the period 1985-1996 from Europe, Australia, New Zealand and the USA.

Less than 1000 tonnes of MBM pa have been imported from European countries, mainly Belgium, France, The Netherlands and Italy, but the species of origin of this MBM is not certain. Importation of concentrate rations is declining from 46-109k tonnes pa in the period 1985-1990 to <10k tonnes from 1993-1996, though not all of the rations contained MBM. Importation was from Europe, South America and Israel.

Scrapie and BSE are notifiable diseases in Cyprus and awareness programmes on the clinical signs of disease for farmers and veterinarians are in place. These employ video recordings, literature and training courses.

Confirmation of TSE is done by microscopic examination of the brain by UK-trained veterinary pathologists. Immunocytochemical detection of PrP is soon to be established in Cyprus but this is currently done in Greece. PrP genotyping of sheep is about to start in order to investigate any association between scrapie occurrence and PrP genotype.

Ruminant protein was prohibited in ruminant rations in Cyprus beginning 14 September 1990. This was changed to mammalian protein on 13 December 1994. The importation of meat and meat products derived from bovine animals slaughtered in the UK is prohibited since 29 March 1996. The importation from the UK of live bovine animals, bovine semen, bovine embryos, MBM and meat meal derived from mammals was prohibited on the same date.
The importation of animal feed, ruminant CNS and ruminant material containing lymphatic tissues from
countries where BSE or (in the case of animal feed) scrapie have been confirmed has been prohibited since
1990. Only certified beef can be imported from countries where BSE has been confirmed, and spinal cord and as
much lymphatic and nervous tissue as possible must be removed.

There are strict controls on the importation of live sheep and goats into Cyprus. They must be ≥42 months old
and come from farms where no case of scrapie or BSE has ever occurred and the flock or herd has been closed
for at least five years. After a period of quarantine in Cyprus the imported ‘ear tagged’ animals are inspected by
the veterinary services for five years, during which time isolation during parturition is mandatory followed by
destruction of placentae and disinfection of the isolation facility.

Waste ruminant products are either buried or ground to a 50mm particle size and rendered at 133°C, 3 bar for 20
minutes.

Ruminant production systems in Cyprus are based on grass feeding. No animal tissues have ever been
incorporated into ruminant feed but this now has the force of law.

Risk assessments for BSE and scrapie have not been initiated.

OIE recommendations have been adopted in regard to BSE and importation of live cattle and cattle products.

CJD is not currently a notifiable disease in Cyprus but preparations to make it so are underway. In the period
1990-1996 there has been only one definite case of conventional sporadic CJD in a 59 year old woman in 1995.
The population of Cyprus is 630,000.

2.2. Jordan

There is a federal structure in regard to animal and public health.

There are three zoos with species of Cervidae, Bovidae or Felidae and all are under State Veterinary control.
Dead animals are buried. No farmed mink exist. No TSE has ever been diagnosed in any animal species in
Jordan.

Around 30,000 cattle (from Germany, The Netherlands, Eastern Europe and Australia), millions of sheep (from
Australia, Bulgaria, Romania and Turkey) and 600 goats (some from Cyprus) have been imported between 1985
and 1997.

Around 70,000 tonnes of bone-in beef, sheep or goat meat has been imported in the same period from eastern
Europe, The Netherlands, Germany, Russia, Sudan and New Zealand.

BSE and scrapie are notifiable diseases in Jordan. An awareness programme for farmers and veterinarians in
regard to the clinical signs of disease utilises video recording, literature and training courses. Facilities for
confirmation of diagnosis by microscopic examination of the brain are in place. Veterinary pathologists have
been trained in the UK and the USA. If other methods are required, suspect material is sent to appropriate
laboratories in the UK.

There is no ruminant protein feeding ban but only plant origin material (mostly cereals) has been fed to
ruminants for a very long time.

There are no offals bans in regard to human consumption but no offals of any description, or products derived
from them, are permitted for animal consumption.

Importation of MBM, live cattle, sheep and goats is only permitted from countries free of BSE and scrapie, in
native-born animals. Goats imported from Cyprus from 1985-1997 were held in quarantine for three years.

Waste ruminant products are incinerated or buried. They are not rendered. There is no legal restriction on the
use of MBM or tallow.

A risk assessment for BSE and scrapie has not been completed and a risk management strategy has not been
adopted. There are no data on the number of cattle brains examined pathologically.
Consumer habits and a lack of quarantine facilities and the appropriate laboratories in Jordan convince the authorities that a zero risk option is in the best interests of the country. CJD is not notifiable and there is no surveillance programme. CJD has not been diagnosed in Jordan in the period 1990-1996. The human population is 4.5 million.

2.3. Kuwait

There is a federal structure in regard to animal and public health.

One zoo exists which houses Cervidae, Bovidae or Felidae species and is under State Veterinary control. Dead animals are incinerated or buried. No farmed mink exist. No TSE has ever been diagnosed in animals in Kuwait.

BSE and scrapie are notifiable diseases. The clinical signs are communicated via an awareness programme using video recording and literature. There are no laboratory facilities for the post mortem confirmation of BSE or scrapie. Brains from any suspect cases are fixed as specified in the Manual of Standards for Diagnostic Tests and Vaccines (Manual) and sent to a TSE reference laboratory.

Bovine CNS, thymus, spleen, ileocaecal part of the intestine and region lymph nodes are not permitted to be used for human or animal consumption.

Live cattle, sheep and goats are imported according to the conditions specified in Chapter 3.2.13 of the OIE International Animal Health Code (Code).

No rendering is done in Kuwait but MBM is completely banned in ruminant feed. There is no restriction on the use of tallow.

A risk assessment for BSE and scrapie has not been done and a risk management strategy has not been adopted. No surveillance or monitoring for BSE has been done in the last five years.

Importation of cattle and cattle products from countries with a high and low incidence of BSE or from countries which have had cases of BSE only in imported cattle is conducted following the OIE Code chapter on BSE.

CJD is a notifiable disease in Kuwait but there is no surveillance programme. No cases of CJD have been reported in the period 1990-1996. The population of Kuwait was 1.75 million in 1996.

2.4. Oman

There is a federal structure in regard to animal and public health.

No pigs or farmed mink exist in Oman and there are no zoos or wildlife parks.

BSE was reported in two cattle in April 1989 which were imported from the UK.

About 200 live cattle were imported from the UK in 1985. Bone-in carcass meat from ruminant animals has been imported from Sudan, Somalia, Australia, United Arab Emirates, India, Germany, New Zealand, The Netherlands, Ireland and the UK.

BSE and scrapie are notifiable diseases.

There is no awareness programme for BSE or scrapie. Confirmation of diagnosis by microscopic examination of the brain is done but veterinary pathologists have not been specifically trained.

There is no ban on the feeding of ruminant protein to ruminant animals and no ban on the feeding of cattle offals to human or animals.

There is a restriction on the importation of live cattle from infected countries.

Rendering is not done. Waste ruminant tissue is incinerated.

A risk assessment for BSE and scrapie has not been done and a risk management strategy has not been adopted. No surveillance or monitoring for BSE has been done in the last five years. Oman does not use the
recommendations in the OIE Code chapter on BSE in regard to the importation of live cattle or the following bovine products: beef, ova, milk and milk products.

CJD is a notifiable disease and a national surveillance programme exists. Two cases of conventional sporadic CJD have occurred between 1990 and 1996 - one in 1993 and one in 1995. No cases of vCJD have been reported. The population of Oman was 2.1 million in 1996.

2.5. Qatar

There is a federal structure in regard to animal and public health.

There is one zoo under State Veterinary control but no farmed mink. Dead animals are incinerated or buried.

No TSE has ever been diagnosed in animals. Since 1990 from a few hundred up to one thousand live cattle have been imported annually from Germany and The Netherlands. In the same period the annual importation of sheep ranges from 40 thousand to 1.5 million from Australia, New Zealand, Syria and Sudan. Goats have been imported from Syria, Jordan and Sudan. The numbers range from zero to 37 thousand per year between 1990 and 1996.

BSE and scrapie are notifiable diseases. An awareness programme on the clinical signs of BSE and scrapie exists. Video recordings and literature are used. There are no laboratory facilities to confirm the diagnosis of BSE and scrapie. Post mortem samples are sent to reference laboratories.

There is no prohibition on the use of ruminant offals for human consumption.

OIE recommendations are followed when importing live ruminant animals, beef, semen, milk and milk products.

No rendering of ruminant waste is done. Such material is exported after initial treatment.

No risk assessment for BSE or scrapie has been made. A risk management strategy has not been adopted.

CJD is a notifiable disease. No cases were reported from 1990-1996 in a population of 650 thousand.

2.6. Saudi Arabia

There is a federal structure in regard to animal and public health.

There are 10 zoos with species of Cervidae, Bovidae or Felidae, all under veterinary control and no known mink farms. Dead animals are incinerated or buried. No TSE has ever been diagnosed in any animal species in Saudi Arabia.

Live ruminant animals, bone-in carcase meat, mammalian meat and bone meal and concentrate rations containing ruminant protein have all been imported since 1985, mainly from Europe and the USA.

BSE, scrapie and all TSE are notifiable diseases in Saudi Arabia. An awareness programme for farmers and veterinarians in regard to the clinical signs of disease utilises video recordings and literature. National facilities exist to confirm BSE and scrapie by microscopic examination of the brain. Veterinary diagnosticians have not received training outside the country.

Prohibition of the feeding of ruminant protein to ruminant animals has been in place since July 1995. The importation and use of meat and bone meal and concentrates containing animal protein has been prohibited since 24 June 1996. Importation of cattle is only allowed from countries free of BSE. Between the years 1989 and 1996 the number of cattle imported by year has fallen from a maximum of 31,308 in 1989 to 6,365 in 1996. Over the same period the annual importation of sheep and goats has varied between 4,948,161 in 1990 and 6,946,102 in 1994.

Waste ruminant products are not rendered.

A risk assessment for BSE and scrapie has not been completed and a risk management strategy has not been adopted. No surveillance or monitoring for BSE has been conducted between 1992 and 1996.

The recommendations, as contained in the OIE Code chapter on BSE have been applied to:
a) bone-in and deboned beef, bovine milk and milk products imported from BSE high and low-incidence countries;

b) the products mentioned in a) with the addition of live cattle, bovine embryos, ova, semen, hides and skins, originating from countries with BSE only in imported cattle.

CJD is a notifiable disease in Saudi Arabia and there is a surveillance programme. No cases of any form of human TSE, including CJD, Gerstmann Sträussler Scheinker disease (GSS) or fatal familial insomnia (FFI), were diagnosed in the period 1990-1996. The population of Saudi Arabia is 18.86 million.

2.7. Turkey

There are three zoos and a small number of mink farms. All are under State Veterinary control. Dead animals from these enterprises are never rendered but rather are incinerated or buried.

TSE has never been diagnosed in any animal species in Turkey.

Between 1986 and 1996 232 thousand tonnes of bone-in carcase meat has been imported from Germany, Austria, The Netherlands and Ukraine.

Live ruminant animals have been imported as follows:

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<thead>
<tr>
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<tbody>
<tr>
<td>Cattle</td>
<td>1.56 million</td>
<td>165 thousand</td>
<td>Mainly from the EU</td>
</tr>
<tr>
<td>Sheep</td>
<td>468 thousand</td>
<td>8.7 thousand</td>
<td>From Austria, Romania, Ukraine and Moldovia</td>
</tr>
<tr>
<td>Goats</td>
<td>300</td>
<td>1103</td>
<td>The Netherlands, Europe</td>
</tr>
</tbody>
</table>

Animal TSE are not notifiable diseases in Turkey. A TSE awareness programme utilises video recordings, literature and training courses.

BSE and scrapie can be diagnosed by microscopic examination of the brain in national laboratory facilities. A new laboratory at Pendik will be able to establish other methods of diagnosis based on detection of PrPSc or fibrils. Veterinary diagnosticians have been trained at Nurenberg, Germany.

Live cattle, sheep and goats for importation must be selected from BSE-free zones of the exporting country. There are no restrictions on the importation of MBM from ruminant animals.

Waste ruminant products are rendered at 140°C for 30-180 minutes at 4-6 atmospheres.

No risk assessment for BSE or scrapie has been done and a risk management strategy has not been developed. No surveillance or monitoring for BSE has been conducted in the last five years.

CJD and other human TSE are not notifiable and there is no surveillance programme for CJD. The total human population is 50-56 million.

2.8. United Arab Emirates

There is a federal structure in regard to animal and public health.

There are two zoos but no farmed mink. Dead animals are disposed of by incineration. No TSE has ever been diagnosed in animals.

Live cattle and sheep have been imported from Europe from 1985 to 1996. Goats have been imported from Cyprus. Bone-in meat from ruminant animals has been imported from Europe between 1985 and 1990.

Neither BSE nor scrapie is notifiable. There are no facilities to confirm TSE diagnosis but post mortem specimens would be sent to a reference laboratory.
There is no ruminant feed ban and no bovine or ovine offals ban for humans or animals.

Importation of live cattle, sheep and goats from the UK has been prohibited since 1990.

Rendering of ruminant waste is done.

No surveillance or monitoring for BSE has been done in the last five years.

The recommendations made in the OIE Code chapter on BSE are not used for live cattle or cattle products because importation is prohibited from countries where the disease has been reported to the OIE.

3. ANIMAL HEALTH MEASURES

3.1. Control of infection in feed

The key animal health measure is to prevent the establishment of new infections via feed. Under natural conditions cattle do not consume cattle tissues directly (other than placenta after parturition) except in parts of the world where cadavers are not removed and where phosphorus or other mineral deficiencies occur and then bones may be consumed. Even in these rare circumstances risks would be unlikely from the bones themselves unless contaminated with CNS tissue from an infected animal. Risks otherwise derive almost entirely from concentrate feed supplements containing MBM derived from ruminant animals infected with TSE agents.

3.2. Infection in bovine tissue (specified risk materials)

If BSE infectivity exists in any bovine animal the highest titre will be in the CNS (brain, eye, spinal cord) and will be highest of all in these tissues from animals with advanced clinical signs of disease. These tissues and possibly parts of the intestine rich in lymphoreticular tissues (e.g. distal-ileum) may be infected in clinically healthy animals challenged experimentally by mouth with BSE-infected brain early (intestine [40]) or later (CNS) in the incubation period. Since animals incubating BSE which are healthy cannot be detected by any practical means, it is necessary to remove these specified risk materials from all older cattle, whether healthy or not, and to dispose of them, ideally by incineration so they cannot enter any feed chain. Removal of these tissues eliminates almost all infectivity at source e.g. in the abattoir or place of processing, such as a knackers yard or hunt kennels. Provided these tissues are kept separate from other usable tissues and are destroyed, the measure will protect other species from exposure to the BSE agent. It is also essential to ensure that the carcases of confirmed cases of BSE are disposed of, ideally by incineration.

3.3. Disposal of risk materials by rendering

In some countries, one way to dispose of specified risk materials and carcases is to render them. If this is done, the process must be validated and shown to reduce BSE infectivity by a sufficient margin. Currently the standard used in the European Union is 133°C for 20 minutes at 3 bar pressure (15). However, this may not be sufficient to guarantee the complete inactivation of the BSE agent in CNS where most of the infectivity is concentrated (38). An improved margin of safety is provided by direct incineration of the carcase and specified risk materials.

3.4. Ruminant feed ban and bovine spongiform encephalopathy in cattle born after the ban was introduced

In the UK the major animal health measure applied was the prohibition of feeding ruminant protein (with certain exceptions e.g. milk) to ruminant animals. If this could have been effectively enforced, it would almost certainly have resulted in the eradication of BSE once the incubation period of already infected animals was complete. As it happened, it was initially neither completely complied with nor effectively enforced (24, 7, 8). Furthermore, certain intricacies of the science were not originally foreseen. Most important among these was the fact that it was not uncommon for ruminant rations to be accidentally cross-contaminated by MBM or by feed for non-ruminants (e.g. pigs and poultry) containing MBM which at that time (up until September 1990) was legally permitted to contain it in the UK.

Secondly, as little as 1g of BSE-infected cow brain was sufficient to infect cattle by the oral route and establish disease four years later (G.A.H. Wells, personal communication). The very small amount required is difficult to
eliminate under commercial conditions. At least this amount of brain could be left in split skulls (from which brain was removed for destruction) and could enter the rendering process, escape destruction and enter feed for non-ruminants via MBM. This was the reason why, in the UK, the original specified bovine offals (SBO)** ban (1989) was extended by specifying unsplit skulls (1995) rather than brain. Over 33,000 cases of BSE in the UK have occurred in cattle born after the feed ban was introduced in July 1988 and most have been caused by these deficiencies. Now fully recognised, they have been eliminated in the UK by prohibition of the use of mammalian MBM in food animal feed, surrender and destruction of existing stocks of MBM or feed containing it, followed by cleaning and disinfection of feed mills and farm feed stores. Also, cattle heads (excluding the tongue) have, since 1996, been identified as specified risk material requiring destruction, thus eliminating virtually any risk that existed previously. Furthermore, carcases (less the skin) of all cattle over 30 months old are also treated as if they were risk material even though most are not.

3.5. Sheep, goats, scrapie and bovine spongiform encephalopathy

The following points are pertinent:

- The emergence of the epidemic of BSE in the UK is consistent with the hypotheses of an increase in exposure to a) scrapie agent and/or b) a cattle-adapted strain of a scrapie-like agent present in the cattle population for some time (46).
- Recycling of infection from infected cattle tissues, via incompletely effective rendering processes and MBM fuelled the epidemic (42) until the ruminant feed ban took effect.
- Sheep and goats are experimentally susceptible to BSE agent in brain material administered orally (18). The spleen in these transmission carries BSE infectivity, unlike in cattle where it is not reported in natural cases of BSE (17).
- The Scientific Veterinary Committee of the EC has examined the results from experimental studies on various rendering processes used in the European Union and challenged with BSE and scrapie infectivity. They have concluded that the process using 133°C at 3 bar for 20 minutes is the most important factor to assure the safety of MBM but this cannot guarantee the complete removal of infection when challenged with high infectivity.
- This process was not used in the UK but changes in the rendering processes in the late 1970s and early 1980s increased the exposure of cattle to the agent (46).

From the above it is clear that in countries with scrapie which feed concentrate rations (that deliberately or accidentally contain ruminant-derived, infected MBM) to ruminant animals run the risk of the following consequences:

- fuelling the occurrence of scrapie in sheep and goats
- establishing BSE in the cattle population with possible risks also for public health
- if no measures are taken, to fuel the BSE epidemic and possibly establish BSE infection in sheep and goats which may also pose a risk for public health.

In studies in the UK there is no epidemiological or other evidence that the BSE agent naturally transmits to sheep or goats.

In order to protect public and animal health from any of these actual or potential risks, the European Commission has specified risk material from cattle, sheep and goats which from 1 January 1998 will be prohibited for use for any purpose (see paragraphs 1.5 and 4.6) (16).

The Commission Decision also prohibits the used of the vertebral column of bovine, ovine and caprine animals for the production of mechanically recovered meat also from 1 January 1998. In the UK, France and some other countries, similar measures have already been taken.

3.6. Need for more than one measure

Experience in the UK has shown that reliance on just one measure (e.g. a ruminant protein feed ban) is inadequate to control a high incidence of BSE. There is a need to have several interlocking controls to ensure the safety of the end product e.g. compulsory slaughter and destruction of clinically suspect cases, a ban on the risk

** SBO at that time included brain, spinal cord, thymus, tonsil, spleen and intestine from all cattle over six months old.
materials from healthy cattle, rendering to a high specification and a mammalian MBM ban, all operated to a very high level of efficiency.

In the UK, where the incidence of BSE was highest, these measures have ensured that the guarantees to protect animal health (cattle and other species) regarding BSE, from a feed source, and public health via a food or other source are as high as any in the world.

3.7. Risks from maternal transmission

The remaining risks for animal health result from those related to maternal or horizontal transmission. Cases of BSE in the offspring of cases have not been reported outside the UK. In the UK epidemic, maternal transmission cannot be detected but if it does occur (1, 36), the incidence is very low and cannot sustain the epidemic. Recent interim analyses of a cohort study reveal that the risk of maternal transmission in the study was just under 10% but the mechanism of transmission was not indicated. It could be: a form of transmission, but there is no evidence to support this from tissue transmission studies, including from milk, placenta, reproductive tissues or embryos; an increased genetic susceptibility to infection in feed; or a combination of each, which hypothesis best fits the data (36). Since the mean incubation period for BSE is five years (1, 31) the average risk to all calves born to infected dams would only be about 1%.

3.8. Risks from horizontal transmission

In regard to horizontal transmission there is little plausible evidence that this occurs on a significant scale. Throughout the UK epidemic the within herd incidence of BSE has remained below 3% (44), which does not indicate contagion. Variation in the PrP gene is also not a major factor in the occurrence of BSE in cattle. The results of a case control study were inconclusive in regard to the occurrence of horizontal transmission (20) as there appeared to be a greater risk for calves born up to three days after a subsequently BSE-affected and unrelated dam calved, than for the calf of the latter. In the UK, since June 1988, parturient BSE-suspect cattle must be isolated for 72 hours following parturition in approved premises, bedding and the non-viable products of conception destroyed and the premises disinfected (39).

3.9. Summary of measures

In summary the main control measures to reduce the risk of BSE occurring should focus upon feed sources of infection. The following should ideally be incinerated:

- Entire carcases of confirmed cases.
- Specified risk materials, notably CNS, from all cattle over a specified age. Alternatively these can be rendered by an approved process at a dedicated establishment and the products burned or buried.
- Non-viable products of conception and contaminated materials from parturient, BSE-suspect cattle. Alternatively these could be buried.

A ban on the feeding of ruminant protein (with certain exclusions e.g. milk) to ruminant animals is essential in countries with BSE and/or scrapie and should be considered elsewhere as recommended by the World Health Organization (49). This usually means the cessation of use of mammalian meat and bone meal in cattle diets or for fertiliser on agricultural land grazed by ruminants. A ban on the use of specified risk materials (notably CNS from cattle, sheep and goats) should be applied to protect other species and to reduce the infection load entering the rendering industry in countries where BSE and/or scrapie occurs.

The processing of waste ruminant tissues and especially CNS from cattle, sheep and goats should be conducted under conditions controlled by the National Veterinary Service using time, temperature and pressures shown experimentally to significantly inactivate the agents of BSE and scrapie. However, it must be appreciated that reliance cannot be placed upon this measure alone as it is not possible to prove that complete inactivation occurs (38).
Importation of MBM or compounded feed that does, or may, contain MBM (e.g. by accidental cross contamination) should only be permitted if certified to conform with a low risk product e.g. by taking account of the country risk, species of origin of the MBM and processing parameters.

Importation of bovine ova or embryos, live cattle and products should be in accordance with Chapter 3.2.13 of the Code (28). This means that offspring of cattle with BSE should not be imported nor should embryos be derived from a donor whose dam has BSE.

Veterinary medical products using bovine tissues in their manufacture or content could present a risk. The guidance offered in Article 3.2.13.13 of the Code (28) should be followed (see also 4.7 below).

4. PUBLIC HEALTH MEASURES

4.1. The risks

There are three main public health risks. These are via:

- Consumption of cattle products from infected animals,
- the use of pharmaceutical, biological, medical or cosmetic products or medical devices containing bovine tissues or using them during manufacture, and
- the occupation.

4.2. The risk from food

If the BSE agent is a human pathogen, for the general public the greatest risk is from consumption of BSE-infected tissues from adult cattle.

The necessary measures follow from the recognition that the main risk comes from CNS tissue and the highest risk is from the CNS of clinically affected cattle.

4.3. Control of risk from clinically affected cattle

Clinically suspect cases must be killed, the brain examined to confirm disease, and the carcase entirely and safely destroyed (49), ideally by incineration.

4.4. Control of risk from infected, clinically healthy cattle

In regard to healthy animals killed for human consumption in countries with BSE or if a significant risk is indicated by a risk assessment, specified risk materials (notably CNS) should be removed from all cattle (other than calves) in the abattoir. These materials should be destroyed so they can enter no food or feed chain (49), ideally by incineration. Alternatively they can be rendered by an approved process and the products burned or buried at an approved site.

4.5. Mechanically recovered meat

Additionally, because under commercial conditions the spinal cord is not, or cannot always be, entirely removed (24), the vertebral columns from cattle (and from sheep and goats) should not be used for the production of mechanically recovered meat as will become the case in all Member States of the EU from 1 January 1998 (16).

4.6. Risks from bovine spongiform encephalopathy in sheep

The risks from BSE in sheep or goats have been mentioned above. To protect public health, where a risk is perceived, rather than relying only upon the species barrier between sheep or goats and man for protection, removal of all sheep and goats with clinical signs of scrapie from all feed chains is paramount (49). Other than the brain (for diagnosis) the entire carcase should ideally be incinerated. Similarly, the CNS of all sheep and goats over one year old and spleen of sheep and goats of any age, whether healthy or not, should be destroyed so they can enter no food or feed chain, as will be the case from 1 January 1998 in the EU (16). The spleen is included because after experimental oral infection of sheep and goats with the BSE agent, infectivity is found in
the spleen as it is in sheep and goats with natural scrapie (17). Scrapie has not been regarded as a zoonosis in over 250 years (4) but since it is not possible to readily distinguish scrapie from BSE in sheep or goats there is a scientific justification for taking this action as part of a risk reduction policy. Such action can be regarded as precautionary but should be reviewed in the light of new information.

4.7. Risks from medicinal devices, products and cosmetics

Risks from the use of medical devices, medical and cosmetic products containing, or using, bovine materials during their manufacture can be reduced to an acceptable level by ensuring that the source is safe using the criteria mentioned in Article 3.2.13.13 of the OIE Code. In addition, wherever practical, the production process should be validated to establish that it is effective in removing, or inactivating, TSE agent infectivity. In Europe, the USA and most other countries government agencies control, to stringent specifications, the production and use of medical, veterinary and cosmetic products.

4.8. Risks from gelatin, collagen and tallow

Gelatin, collagen and tallow are sourced from animal tissues, particularly cattle. They are used in a wide variety of food, pharmaceutical and cosmetic products and for technical purposes. There is world-wide production on a very large scale for gelatin and tallow. These three products have been carefully scrutinised by various committees and organisations including the UK Spongiform Encephalopathy Advisory Committee (SEAC), the EC, the WHO and the OIE. The same principles, in regard to safety, apply to biologicals, pharmaceuticals and cosmetics, namely to ensure safe sources are used.

The source materials for gelatin and collagen are mainly bone and skin which, even from cattle with clinical signs of BSE, show no detectable infectivity. Inherently therefore, these tissues have a low risk. However, skulls and vertebral column could still contain residual spinal cord which, if from an animal in the late stages of BSE incubation, may contain infectivity. Some countries, notably the UK, have ensured these bones are not used for gelatin manufacture rather than relying upon the severe chemical processes, filtration and heat treatments alone for inactivation and removal of any infectivity. Validation of these processes is under study.

Natural bovine fat from BSE-affected cattle is devoid of detectable infectivity (26). Furthermore, tallow, even that produced from BSE-spiked raw material via rendering processes that are ineffective at inactivating the BSE agent in MBM, shows no detectable infectivity. Accordingly, tallow originating from healthy animals in any country can be traded without restriction (28).

4.9. Occupational risks

Some individuals may be of greater risk of exposure to BSE or scrapie agents by virtue of occupation. There seems to be no definitive link between occupation and CJD or vCJD occurrence. The risk to farmers, for example, is similar in the UK, which had a high incidence of BSE, to that in other European countries with no or low incidences of BSE (11, 12, 48). Other occupations that are more likely to have received higher exposure to BSE than the general population include veterinarians (especially pathologists), TSE research workers, personnel who work in the abattoir, rendering, cattle disposal industries and butchers. All personnel at increased risk of exposure should be provided with information as to the risks and guidance on how to reduce or eliminate them.

5. THE PROBLEM FOR COUNTRIES BELIEVED TO BE WITHOUT CASES OF ANIMAL TSE WITH SPECIAL REFERENCE TO BSE

5.1. The problem

There are three reasons why responsible government authorities need information in regard to the occurrence of TSE in animals: first and foremost, to ensure that adequate protection of public health is secure; second, to protect animal health, including species other than ruminants; and third, to protect the trading position in relation to other countries so there is no disadvantage.

In all countries other than the UK, BSE is a low incidence disease and it is rapidly also becoming so in the UK as a result of the BSE eradication programme. If BSE exists in countries believed to be free of the disease it will only be detected by continuous surveillance and monitoring for the disease. The mean incubation period of five years, means that, even if a case is detected, other individually undetectable, infected cattle may already have been consumed especially if any form of infection recycling takes place.
The risk of BSE occurrence cannot be entirely eliminated. However, the risk of development of an epidemic can be reduced to a very low level by conducting a risk assessment and then preparing and implementing a risk management policy.

Risks exist in Middle East Region countries even though not a single case of BSE has been reported in native-born animals. Risks are apparent from the answers to the questionnaires reported in Section 2.

5.2. Exogenous risks

Risks can be exogenous - arising outside the country - and thus can be prevented by control of importation of live cattle and cattle products coming from at-risk countries as recommended by the OIE Code (28). It is not necessary to prevent importation but rather to ensure the risks are kept to a minimum by setting standards for certification. The main risks arise from the importation of live animals (including offspring of BSE affected animals) or of feedstuff containing MBM derived from ruminants. It is very important to appreciate the risk of accidental cross contamination of ruminant diets in mills and on farms, even if the imported feedstuff is not intended to be fed to ruminants. This is often overlooked. To date, there is no direct evidence that embryos from cattle with BSE carry BSE infectivity. The OIE Code (28) explains how to reduce any risk there may be from the importation of bovine embryos and ova to an acceptable level whilst still permitting genetic improvement.

5.3. Endogenous risks

Risks can also be endogenous i.e. arising from within the country. Three main risks exist:

- to cattle (and other ruminants) from infected feed,
- to man and animals from the specified risk materials (notably CNS) or products from them used for consumption,
- from products of rendering produced by processes which do not inactivate the agent.

Experience suggests that whereas exogenous risks are generally responded to, those from endogenous sources are under-estimated and leave a potentially dangerous situation that would be exploited by the BSE agent should it ever arise.

5.4. Risk assessment and management

As described in the OIE Code chapter on BSE (28), for countries to be considered free of BSE a risk assessment on the above lines must be conducted and a management strategy adopted to address any risks identified. Other conditions are specified in Article 3.2.13.2 and include making BSE a notifiable disease and ensuring an effective and continuous monitoring system as specified in Article 3.2.13.1 is practised.

5.5. Creutzfeldt-Jakob disease surveillance and monitoring in the Middle East

The incidence of CJD in the countries submitting reports is low and not in excess of that existing elsewhere in the world. No cases of vCJD have been reported. It is probable that ascertainment of CJD cases could be improved by continuous surveillance and monitoring by a central authority in each country. This could be of value should a direct connection between BSE and CJD (including vCJD) be made elsewhere in the world.

5.6. Conclusion

From the above it is clear that further action could reduce the risk of BSE occurrence in some countries. If risks are reduced it would probably enable BSE to be eradicated from the world, thus protecting both public and animal health. Control, and eventual eradication, of BSE in cattle will result in a very low risk for humans and is likely to be the most important method of maintaining and improving confidence in beef and beef products worldwide.

REFERENCES


