Risk management of transmissible spongiform encephalopathies in Europe

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Summary
Bovine spongiform encephalopathy (BSE) was first described in the United Kingdom (UK) in November 1986. After the introduction of an active surveillance system, most countries in Europe have reported BSE cases in the cattle population. This indicates that the use of active surveillance in addition to passive surveillance is important to assess the true BSE status in a country.
Scrapie, a transmissible spongiform encephalopathy (TSE) in sheep and goats, has been reported in countries throughout the world with a few notable exceptions. Concern was expressed that BSE could have been introduced into sheep and goats. Currently, distinguishing between scrapie and BSE in small ruminants is only possible through lengthy experiments in mice. Preliminary results of active surveillance, introduced in 2002, show that significant under-reporting occurred.
The history of BSE in cattle shows that risk assessments concerning the risk in a given country were often ignored and subsequent risk management decisions were inaccurate, i.e. although the risk was probable, no measures were taken in terms of either animal or human health. Furthermore, the effect of the measures taken was often overestimated and these had to be amended several times. The most important action to prevent new cases of TSEs occurring is by banning the feeding meat-and-bone meal (MBM) to ruminants. Further measures to be considered are the exclusion of specified risk material and carcasses from rendering, the process parameters for rendering of animal waste and the prevention of cross-contamination of feed with MBM. The most important measures to protect the consumer are the ban on specified risk material, such as brain and spinal cord, which may contain particularly high concentrations of the BSE agent, and the ban on mechanically recovered meat.
The most important measures taken in Europe and the scientific background thereof are described and discussed.

Keywords

Introduction
After the discovery of bovine spongiform encephalopathy (BSE) as a new disease in 1986, countries other than the United Kingdom (UK) took some years to realise the importance and the potential threat of this new cattle disease to their own livestock industries.
The UK was the first country affected with BSE (91) and is the only country in which a large-scale epidemic has occurred.

However, it has been increasingly shown that the disease is not a purely British problem and more and more countries in Europe have detected BSE in their herds over the years since 1990. A targeted surveillance system in risk populations was implemented in several countries in Europe in 2001. As a result, countries that for years were considered BSE-free have subsequently detected the disease (66).

Scrapie was first recognised as a disease of sheep in Great Britain and other countries of western Europe more than...

Risk management of bovine spongiform encephalopathy in cattle in Europe

The most important measures taken include the detection (surveillance) and elimination of infected cattle before slaughter, the ban on specified risk material (SRM) in feed, adequate processing of animal wastes, the ban on feeding meat-and-bone meal (MBM) to ruminants, the ban on SRM in food and restrictions on imports (Fig. 1).

Surveillance

Before recognition of the occurrence of BSE, neuropathological examinations of cattle were rare except in regions where rabies was a problem. The spread of BSE in the UK first went unnoticed because most infected cattle were slaughtered before showing clinical signs of the disease and the clinical signs that appeared were similar to those observed in other bovine diseases. Farmers were also unlikely to request a post-mortem examination for a single sick cow. In September 1985, the first case of spongiform encephalopathy diagnosed in a cow was concluded to be probably caused by a toxic effect. The fact that

250 years ago (57). The disease has been reported in most sheep-raising countries throughout the world with few notable exceptions (67). However, although the disease has been known for a long time, surveillance in most countries is insufficient and no adequate strategy to eradicate the disease exists. There is no scientific evidence to indicate that scrapie poses a risk to human health (50, 53). The successful experimental oral transmission of BSE to sheep in 1993 (43) opened another chapter. The crucial question as to whether the BSE agent is naturally transmitted to small ruminants has still not been answered to date. However, currently, no practical assay exists, which could readily distinguish small ruminants infected with scrapie from those infected with BSE (71). The established technique requires lengthy studies in mice injected with brain material collected post mortem from positive small ruminants. The wide distribution of the transmissible spongiform encephalopathy (TSE) agent in different organs in small ruminants, together with the impossibility of discriminating clinically or pathologically (8) between scrapie and BSE in sheep, may constitute an additional risk of introducing BSE-infected material into the human food chain. The recommendation following the Joint World Health Organization (WHO)/Food and Agriculture Organization (FAO)/Office International des Epizooties (OIE: World organisation for animal health) Technical Consultation on BSE in June 2001 (64) was that in countries where sheep and goat populations have been potentially exposed to BSE, measures should be taken to minimise exposure of humans to infectivity from small ruminants.

Ideally, risk management should be based on risk assessment. The measures chosen as an outcome of the risk assessment process should be scientifically justified and if significant uncertainty exists, a precautionary approach may be adopted. However, the measures selected must nevertheless be based on a risk assessment that takes account of the available scientific information (59). Given the many unknown factors, adequately assessing a situation and taking the right measures is sometimes difficult. Public perception and politics also influence the measures taken.

The effect of measures implemented can only be judged after the average BSE incubation period. Measures therefore have to be revised and updated year by year, not only because new scientific data become available, but also because experience often shows that the measures implemented were not fully effective.

Risk management in Europe – including more than 40 countries – is generally not harmonised. The European Union (EU), comprising 15 member states, and Norway have common rules and some of the countries wanting to join the EU are adapting their measures accordingly. However, implementation of these measures varies considerably from one country to another (41). The following observations thus focus mainly on the most important measures taken in the EU.
A new disease had begun to emerge was not recognised until the end of 1986 following the submission of more brain samples with this unusual pattern. The occurrence of the new disease was finally published in a scientific journal in 1987 (1).

The lack of case reports underlines the need to publish and inform farmers, veterinarians and other related professions of such unusual events at as early a stage as possible. A surveillance system can only be initiated with knowledge about a new disease. Early detection can be followed by an early response, thereby allowing the spread of the disease to be contained.

**Passive surveillance**

Passive surveillance is based on the reporting and subsequent investigation of clinically suspected cases. For important diseases such as List A diseases, this reporting of clinical suspicion is often made mandatory. However, the true incidence of several diseases is underestimated by passive surveillance (55, 90).

All bovine animals suspected of being infected with BSE should be subjected to laboratory examinations, because merely declaring the disease as statutorily notifiable is insufficient.

A passive system for detecting BSE is relatively subjective and depends on several factors, as described below.

Herdsmen, veterinarians, slaughterhouse personnel and others handling cattle play a crucial role in any surveillance system and need to be fully aware of the clinical signs of BSE. For a long time, it was thought that a suspected case of BSE could be readily diagnosed based on clinical signs. Pictures on television and in other media always showed cows in the end-stage of the disease. Such animals display behavioural changes including apprehension, frenzy and nervousness, abnormalities in posture and movement most commonly observed as ataxia, tremors and falling. They also show changes in sensitivity, mainly exhibited as hyperaesthesia to sound and touch. With this picture of BSE prevailing in many countries, most cases were often overlooked because such drastic clinical signs are normally only observed at the end-stage of the disease: Clinical cases may thus be missed as a result of preconceived ideas as to the appearance of BSE. It is therefore important that veterinarians, farmers and other professionals be continuously familiarised also with the subtle clinical signs of a BSE case. Veterinarians must be encouraged to notify veterinary authorities of all cattle with neurological disorders for specialised pathological examination and the notification procedure should be made clear and easy, so that all the parties involved know how to react when confronted with a suspected case.

Another important issue is willingness to report suspected cases. Motivation to notify depends on the measures taken – if these are too strict and not based on adequate scientific data, motivation to notify is low. One example is the set of measures taken in herds where a BSE case has occurred. Some countries which practise herd-culling observed a marked unwillingness among farmers to report cases, mainly because of the psychological problems associated with losing ‘a life-long investment’ rather than because of any financial losses. Presenting a persuasive case to a farmer requesting scientific arguments to explain why young calves purchased a year earlier have to be culled is a difficult task when the only answer is a bureaucratic one.

Motivation to notify is further influenced by the compensation paid. Full compensation of the value of the animal and of all the costs related to management of the case, such as diagnosis, the visit of the veterinarian, incineration and any other costs is essential. It is also important that compensation be paid immediately and not several months later. Surprisingly in the UK, no significant increase in reporting was observed when, in February 1990, compensation paid to farmers was raised from 50% to 100% of the market value of the animals (85).

Furthermore, the stigma associated with BSE should not be underestimated. Especially with the first cases of BSE detected in a country, the farmers affected are often treated as ‘bad farmers’ and the children of these farmers have been known to experience problems at school. This psychological pressure can only be avoided by proactive information and communication, which had never been practised in countries in Europe before the first case occurred.

Another important issue is the competence of the laboratory used for diagnosis, which should be aware of all the BSE-
diagnostic methods available. A laboratory which has suitably trained pathologists and which is consequently capable of diagnosing BSE is therefore of paramount importance.

With a passive surveillance system, the detection rate of a disease can be variable and the results difficult to interpret and compare between countries. In recent times, it has become increasingly obvious that a passive surveillance system alone, based on the notification of suspected cases, is insufficient to provide evidence of freedom of a country from BSE. However, passive surveillance is an important part of any surveillance system. Analysis of the BSE tests performed in the EU in 2001 (38) shows that 51% of positive cases were detected by passive surveillance. This highlights the importance of passive surveillance as part of the whole system. Nevertheless, in some EU member states, passive surveillance seems inexistent. In 2001, the number of suspected cattle in the countries of the EU and Switzerland varied between 2 and 408 per million adult cattle (Table I). Interestingly, the first reports of the occurrence of BSE in an affected country increased disease awareness drastically.

### Table I

<table>
<thead>
<tr>
<th>Country</th>
<th>Suspects per million adult cattle</th>
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<tbody>
<tr>
<td>Austria</td>
<td>2</td>
</tr>
<tr>
<td>Belgium</td>
<td>161</td>
</tr>
<tr>
<td>Denmark</td>
<td>81</td>
</tr>
<tr>
<td>Finland</td>
<td>8</td>
</tr>
<tr>
<td>France</td>
<td>43</td>
</tr>
<tr>
<td>Germany</td>
<td>32</td>
</tr>
<tr>
<td>Greece</td>
<td>10</td>
</tr>
<tr>
<td>Ireland</td>
<td>142</td>
</tr>
<tr>
<td>Italy</td>
<td>3</td>
</tr>
<tr>
<td>Luxembourg</td>
<td>140</td>
</tr>
<tr>
<td>Netherlands</td>
<td>54</td>
</tr>
<tr>
<td>Portugal</td>
<td>408</td>
</tr>
<tr>
<td>Spain</td>
<td>28</td>
</tr>
<tr>
<td>Sweden</td>
<td>36</td>
</tr>
<tr>
<td>Switzerland</td>
<td>183</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>228</td>
</tr>
</tbody>
</table>

In the UK, BSE and scrapie were declared notifiable diseases in 1988 and 1993, respectively. Once evidence showed that BSE was not restricted to the UK, reporting of suspected clinical cases of BSE became mandatory in most countries in Europe. Switzerland made BSE and scrapie notifiable on 1 December 1990 and the EU on 1 April 1990 (16) and 1993, respectively.

### Active surveillance

Until 1999, the only method used to identify suspect cases of BSE was based on the reporting of clinically suspected cases, i.e. of cattle displaying clinical signs compatible with BSE.

With active surveillance, statistically representative numbers of animals are identified from defined target populations and these animals are then tested for the disease under investigation. This is often referred to as targeted screening (12).

Histopathology and immunohistochemistry are established and reliable methods for confirming BSE in cattle, but the procedures are cumbersome, time-consuming and therefore not suited for the mass testing of animals.

Validated rapid BSE tests are available (58), permitting fast and uncomplicated testing of brain tissue for BSE on a large scale and identification of infected animals in the last stage of the incubation period. This has made implementation of active surveillance programmes possible in populations at risk. Unfortunately, these tests are not sufficiently sensitive to identify animals that, although being infected, lack the concentration of BSE agent in the brain required for detection. A negative result is thus no guarantee that a tested animal is not infected. Nevertheless, the use of these tests has resulted in a better estimation of the true incidence of BSE and they have proved to be a useful screening technique, although the confirmatory test procedure for BSE remains histopathology and immunohistochemistry as described in the OIE Manual of Standards for Diagnostic Tests and Vaccines (63).

With the availability of a screening test for BSE, Switzerland introduced a targeted surveillance scheme in risk populations at the beginning of 1999 to enhance detection of BSE cases in the adult cattle population (11, 13). In addition to the mandatory reporting of all suspected clinical cases, all fallen or killed adult cattle and all cows slaughtered in emergency are investigated. The population most likely to yield BSE cases was assumed to be fallen adult cattle. This population comprises animals that are too ill to be slaughtered, wasting or dead animals and animals that do not recover after treatment. Animals slaughtered in emergency were estimated to be the second most likely population to yield BSE cases, since these animals were ill or had had an accident prior to slaughter. In addition, a random sample of routinely slaughtered cattle is examined. The first results of this surveillance scheme indicated that the risk population chosen was very useful for detecting additional cases of BSE. Based on the Swiss experience, France introduced a similar surveillance approach in spring 2000 in part of the country and confirmed the validity of the scheme.

An active surveillance system has now been implemented in many countries in Europe. Since January 2001, the EU
practises the systematic screening of cattle for BSE (27, 35, 36, 40), according to the following categories:

– a random sample of fallen stock, i.e. animals which die or are killed on the farm or during transport aged >30 months, was initially tested. However, in July 2001, it was decided to test all fallen stock aged over 24 months for one year. This measure was to be revised on the basis of experience gained during the first six months. The provision was prolonged in July 2002

– all emergency slaughtered cattle aged >30 months are tested, i.e. animals which have suffered an accident or display serious physiological and functional problems, animals which are suspected at ante-mortem inspection to be suffering from a disease communicable to man and animals, animals displaying symptoms or the general condition of which indicates that such a disease may occur, or animals showing symptoms of a disease or a disorder of general condition likely to render their meat unfit for human consumption. The age for testing was changed to >24 months from July 2001

– all normally slaughtered cattle aged >30 months are tested. Some member states also decided to test routinely slaughtered cattle aged >24 months while in other member states, testing was extended to animals aged <24 months, e.g. Germany tested healthy slaughtered cattle aged <24 months which accounted for 25% of the tested cattle. Austria, Sweden and Finland allowed a derogation for regular slaughter practices on their national markets until June 2001. They then allowed random testing of samples. Since April 2002, the derogation is only valid for Sweden.

The results of this testing scheme in the EU are published regularly (42) and confirm that the risk groups identified – fallen stock and emergency slaughter – were suitable for targeted surveillance (Table II). A total of 8,516,227 bovine animals were tested in the framework of the monitoring programme in the EU in 2001, 2,153 of which proved positive (38), 49% of positive cases were detected by active surveillance. In several countries, all or most of the BSE-positive cattle were detected by active surveillance. In these countries, disease awareness or willingness to report cases seems insufficient. Although the largest numbers of tested cattle in the EU are normally slaughtered cattle, the majority of positive cases occur in the suspected cases and risk populations (fallen stock and emergency slaughter) (Table II).

Table II
Ratio of bovine spongiform encephalopathy-positive animals per 10,000 cattle in the various populations tested in the European Union in 2001

<table>
<thead>
<tr>
<th>Cattle tested</th>
<th>Ratio: positive animals per 10,000 cattle tested (minimum and maximum ratio)</th>
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<tbody>
<tr>
<td>Normal slaughter</td>
<td>0.36 (0.6-89)</td>
</tr>
<tr>
<td>Risk population</td>
<td>9.74 (0.5-52.57)</td>
</tr>
<tr>
<td>Clinical suspects</td>
<td>3376 (0.6590)</td>
</tr>
</tbody>
</table>

Conclusions on surveillance

An efficient surveillance system can provide important clues to the true incidence of TSE. Following the introduction of active surveillance, BSE was detected in some countries considered BSE-free for years (Austria, Czech Republic, Finland, Germany, Greece, Israel, Italy, Japan, Poland, Slovak Republic, Slovenia and Spain) and in other countries, the incidence of the disease has increased dramatically (Belgium, France, Ireland, Netherlands, Portugal and Switzerland). The absence of reported cases should therefore not automatically be equated with freedom from BSE.

In summary, a system combining passive and active surveillance is required. An effective surveillance system is not only crucial for detection of the true incidence of BSE, but also for evaluating the effect of the measures implemented.

Animal health measures

Feed bans

Extensive epidemiological studies have traced the cause of BSE to animal feed containing inadequately treated ruminant MBM (solid protein products obtained when animal tissues are rendered, in particular meat-and-bone meal as such, meat meal, bone meal and greaves) (96, 97). Although some elements of the story are still disputed (agent originating from scrapie, endemic BSE or another cause), changes in the rendering process used around 1980 probably allowed the aetiological agent to survive, contaminate the MBM and infect cattle. Some of the infected cattle, slaughtered at an older age, could have shown early signs of BSE if they were approaching the end of the BSE incubation period. In such cases, while still preclinical, the cattle would have harboured infectivity similar to that observed in clinical cases of BSE. The cattle carcasses and wastes thereof were then recycled through the rendering plants, increasing the level of the pathogen – which by now had become adapted to cattle – in the protein supplement, thus causing a BSE epidemic. Recognition of this source of infection led to the banning of feeding MBM to ruminants, to break the cycle of cattle re-infection.

The occurrence of BSE cases after the implementation of the feed ban in ruminants and exclusion of SRM in feed has mandated the introduction of further measures. Even when no MBM is included in ruminant feed, the agent may still be recycled through cross-contamination and cross-feeding. These traces may result from cross-contamination of MBM-free cattle feed with pig or poultry feed containing MBM, e.g. from feed mills that produce both types of feed in the same production lines, from transport by the same vehicles and from inappropriate feeding practices on farms. Apparently, flushing batches in feed mills, which is often used as a safeguard against such cross-contamination, is not sufficient. The traces of MBM detected in countries in Europe are most often below 0.1%, which seems to be sufficient to infect cattle. Dedicated
production lines and transport channels and control of the use and possession of MBM at farm level would be required to completely control cross-contamination. As long as feeding of MBM to other farmed animals is possible, cross-contamination of cattle feed with MBM is very difficult to eliminate. A more stringent option, therefore, consists of banning the feeding of MBM to all farmed animals.

Feed bans implemented in Europe
Ruminant MBM was banned for use in ruminant feed in the UK in July 1988 and the ban was extended to mammalian MBM in November 1994 (4).

The EU banned the feeding of mammalian MBM to ruminants in 1994 (18). Some countries, which reported BSE cases in the early 1990s, banned MBM before 1994 (Table III). In some cases, a feed ban on ruminant MBM to ruminants was implemented as the first step. The ban was then extended to mammalian MBM due to the difficulty in distinguishing between MBM of ruminant origin and MBM of non-ruminant mammalian origin. This decision made it easier to control the feed ban. Only a few countries without reported cases of BSE at that time (e.g. Sweden, Finland, Netherlands and Denmark) banned the feeding of MBM to ruminants before the EU decision. Most countries did not see the need to implement a feed ban for ruminants – either they felt themselves not at risk or they trusted in the assumption that cattle have never traditionally been fed MBM.

Due to the difficulties of avoiding cross-contamination of cattle feed with MBM, most countries in Europe introduced a total feed ban (feeding of MBM to all farm animals) in 2001 (29).

Processing animal waste
Until 1990, knowledge about the capacity of rendering processes to inactivate the pathogen was limited, even though early inactivation studies showed that the TSE agent is extremely resistant to most physical and chemical inactivation methods (54, 86, 87). A research project imitating rendering practices demonstrated that only a batch system using 133°C at a pressure of 3 bar for 20 min was effective (88, 89). Based on these results, the EU imposed process parameters of 133°C at a pressure of 3 bar for 20 min. Although the process is relatively effective, scientific research has proven that even if such stringent parameters are used to treat infected material, the BSE agent is not completely inactivated. These parameters therefore do not guarantee absolute freedom from infectivity of MBM in cases where material with high levels of BSE infectivity enters the rendering process.

Processing parameters implemented in Europe
In some countries in Europe, the standard of 133°C at a pressure of 3 bar for 20 min had already been used for decades, but was not a legal requirement. This standard had already been applied in principle since 1990 for high risk material (fallen stock) (17). The EU passed a resolution in 1996, which was implemented in 1997, to introduce the rendering parameters of 133°C at a pressure of 3 bar for 20 min for all mammalian waste used for the production of MBM, except bones fit for human consumption (20). The same process standard was introduced in 2000 for the rendering of bones fit for human consumption, including the vertebral column and often the skull.

Ban on specified risk materials in feed
In the early 1990s, infectivity studies of BSE in cattle were not complete. Only infectivity in the brain had been detected at that time through BSE-inoculation in mice (7, 45). The list of SRM to be excluded was, at that time, therefore mainly based on scrapie-infectivity studies.

Scrapie replicates primarily in the lymphoreticular system. Infectivity has been found in numerous lymph nodes, the tonsils, the spleen, in lymphoid tissue associated with the intestinal tract and placenta, and during the later preclinical phase, in the central nervous system (47, 48, 49, 68). In addition to the lymphoreticular and central nervous systems, infectivity has also been detected in the pituitary and adrenal gland.

Table III
<table>
<thead>
<tr>
<th>Measures</th>
<th>European Union</th>
<th>Great Britain</th>
<th>Ireland</th>
<th>Portugal</th>
<th>France</th>
<th>Switzerland</th>
</tr>
</thead>
</table>
glands, the bone marrow, pancreas, thymus, liver and in peripheral nerves (46, 47, 48, 49).

The first results of BSE infectivity, based on studies in which mice were intracerebrally inoculated with tissue from BSE field cases and from cattle experimentally infected by the oral route ('pathogenesis study'), became available in 1996 (93).

To date, in field cases of BSE-infected cattle, infectivity has only been recorded in the brain, spinal cord and eyes. In experimentally-infected cattle, BSE infectivity has been found in the distal ileum at intervals during the incubation period starting six months after exposure (92). Furthermore, central nervous tissues and dorsal root and trigeminal ganglia (77, 94) were found to be infective shortly before the onset of clinical signs. In one study, sternal bone marrow collected during the clinical phase of disease was found to be infective, but one of the possible explanations for this case is that infectivity might have been due to cross-contamination of the tissues (95). Recently, infectivity was detected in the palatine tonsils of cattle infected experimentally by intracerebral inoculation (6).

Some material, such as the brain and spinal cord, may contain particularly high concentrations of the BSE agent. If these materials – both from imported and from domestic cattle – are removed at slaughter and then incinerated, the risk of recycling the pathogen is markedly reduced. If these materials are processed for further use in animal feed, there is a high risk of amplification of the BSE agent. In addition, to remove infectivity from the feed chain, fallen stock should not be recycled.

**Ban on specified risk materials in feed implemented in Europe**

Before 1990, there were no bans on SRM in feed. The first successful intracerebral transmission of BSE to pigs (10) caused the UK to institute a ban on the use of SRM in feed for all species in 1990. At that time, the list of SRM included the brain, spinal cord, tonsils, thymus, spleen and intestines from cattle aged over six months. In November 1994, following detection of the BSE agent in the ileum of calves six months after infection, the ban was extended to the intestines and thymus in calves under six months of age (92). Removal of the brain and eyes from the skull was forbidden in August 1995.

Other countries with reported BSE reacted very differently. Switzerland excluded SRM for human consumption after the occurrence of BSE in the country. The animal feed chain, however, was not part of this exclusion. Except for the UK, none of the countries in Europe implemented the ban on SRM in feed before 1996 (Table III).

In 1997, as a precautionary measure, the EU Commission proposed to ban SRM from cattle (22) not only in EU member states with BSE, but also in other EU member states with no cases of BSE. Most member states with no reported cases of BSE were opposed to this ruling. Finally, in June 2000, an agreement was reached on EU general rules for the use of SRM (28). These rules, which have been in force since 1 October 2000, provide a common list of cattle, sheep and goat materials which have to be removed and destroyed as SRM. The list of bovine tissues is slightly longer for Portugal and the UK. The list of tissues was slightly extended (30, 32, 33, 34) following further evaluation of scientific evidence by the SSC. These decisions added the intestines of bovines of all ages and the vertebral column from bovines over 12 months to the list of SRM. Furthermore, since the beginning of 2001, including dead animals (fallen stock) in the production of feed for farm animals is prohibited (31).

**Discussion of the animal health measures**

The history of the feed measures taken shows that some of these were insufficient to completely prevent recycling of the BSE agent. The measures were therefore amended several times, based on new scientific findings and experience gained.

The effect of the measures concerning feed can be assessed by the number of BSE cases which occurred subsequently (Fig. 2). As early as 1992, the OIE recommended banning the feeding of ruminants with MBM derived from ruminants (62). This recommendation was described as the key requirement for eliminating the possibility that cattle might be exposed to the BSE agent through their feed and also suggested that countries without BSE cases might consider a feed ban.

The feed ban for ruminants was regarded by far as the simplest way to prevent BSE (52). This was the only ban implemented in countries with BSE reported immediately and was also accepted by EU member states without cases of BSE in 1994 (18). Nevertheless, most countries did not take implementation of the feed ban very seriously (41) and the controls carried out were not very convincing. Feed control is not easy, because the only currently available and validated method consists of detecting bone fragments by microscopy. This method requires experience and is very elaborate. For a long time, no measures were taken despite the fact that traces of MBM were detected in cattle feed.

Nevertheless, the ruminant feed ban did have an effect, as can be seen from the reduced number of BSE cases in cattle born after the ban, both in UK and Switzerland. The ban, however, was insufficient to reduce the rate of new infections among cattle to negligible numbers. Complete eradication of BSE therefore required additional measures. In France, no visible effect was observed following the ruminant feed ban, mainly due to inadequate surveillance at that time. This indicates the need for adequate surveillance to judge the effectiveness of the measures implemented.
The effect of applying the process parameters of 133°C at a pressure of 3 bar for 20 min to the treatment of animal waste is difficult to judge. One of the crucial problems is that bones – which contain vertebral columns and in some countries, skulls, including the brain – had not been treated under these conditions.

The banning of SRM in feed was also implemented at a surprisingly late juncture by countries with reported cases of BSE. The predominant opinion was that the ruminant feed ban, together with the process parameters of 133°C at a pressure of 3 bar for 20 min, should be sufficient for a country with a low incidence of BSE to prevent amplification of the disease. The reporting of cases of BSE in cattle born after implementation of these measures proved the contrary (Fig. 2). Implementation of the SRM ban in feed also served to reduce infectivity, but did not reduce it to zero, mainly due to the problem of cross-contamination and cross-feeding.

The first reporting of cases of BSE in several countries in Europe in the winter of 2000 to 2001 led to a crisis. Implementing harsh measures, such as the total ban on feeding MBM to all farm animals, only became possible in this critical situation. The impact of the total feed ban cannot yet be fully judged, but the situation in the UK is promising – to date, only approximately seventeen cases have occurred after the total feed ban (3).

Whether the total feed ban is a sustainable solution is questionable. More than 50% of the total weight of each cow is not used for human consumption, but only a small part of these tissues may potentially contain infectivity. Despite this fact, a vast amount of valuable protein and tallow is incinerated due to the total feed ban. Improvement of control and analytical methods, as well as some innovative ideas are urgently required.

**On-farm measures**

According to present knowledge, BSE is not transmitted from cow to cow. However, other cattle may also have consumed feed from a contaminated feed batch.

The objective of any culling is to eliminate animals epidemiologically linked to an index case with the aim of avoiding future cases of BSE by reducing the risk of infected animals entering the feed and food chain. To achieve this objective, a culling scheme must target those animals which carry the highest risk of being infected despite not showing signs compatible with BSE.

The main culling schemes that were and still are applied in countries in Europe are listed below. The approach is slightly different in each country.
Depending on the country, culling varies as follows:
- only the index case
- all cattle on case farm
- all cattle on original farm
- all cattle on case and original farm
- all susceptible animals on the farm (including cats)
- ‘feed cohort’
- ‘birth cohort’ (born one year before and after the BSE-infected animals, born and raised on the same farm).

The feed cohort, i.e. the animals that could have been exposed to the same feed as a confirmed case, would be the ideal approach, but is impossible to evaluate (74). In reality, identifying this target population is also often impossible because the potentially contaminated feed batch can usually not be identified and the contaminated feed will most likely have been given to several herds. Distribution of the BSE agent within the contaminated feed batches is also not known. In Belgium, efforts were made to identify feed cohorts. Given the above-mentioned uncertainties, the result was that about 50% of the Belgian national herd could theoretically have been exposed, which shows that the approach of targeting animals potentially exposed to the same feed as the index case would seem unrealistic.

Data from Germany, France, Portugal, Spain, Switzerland and Ireland showed that all secondary cases detected when testing animals culled under the herd-culling scheme belonged to the birth cohort, i.e. born within 12 months of the birth of the affected cattle of the index cases (74, 79). Based on these data, culling can be concluded to reduce the incidence of BSE. Cohort-culling seems to be a more effective approach than herd-culling.

Vertical transmission is theoretically a possible route of transmission since this appears to occur in natural scrapie in sheep. There is some statistical support for the possibility that some form of maternal transmission of BSE takes place in cattle (9, 14, 15, 98). However, if such is the case, vertical transmission cannot account for more than 10% of the offspring of all cases with BSE and probably less if transmission to calves occurs only in those cases where the dam is in the late stage of BSE incubation. Furthermore, there is no evidence to date that this so-called ‘maternal transmission’ occurs in the absence of a feed-borne source, and no plausible mechanism for this type of transmission has been identified. Nevertheless, maternal transmission is currently impossible to exclude completely as an occasional cause of BSE (76).

**On-farm measures implemented in Europe**

Since 1996, most countries have practised culling the whole herd of animals affected with BSE. Today, the EU requirement (35) is that all other bovines on the holding of the animal in which the disease has been confirmed are to be culled and destroyed. This also allows member states the option of deciding not to kill and destroy all these animals, depending on the epidemiological situation and traceability of the animals on that holding.

In practice, many countries in Europe have changed their approach of culling animals in BSE herds. Most use the birth cohort approach, which means that they cull only cattle born within 12 months of the birth of the affected cattle in the herd in which the affected animal was born and reared. Some countries use a different approach, such as France, where all cattle on the farm born before January 2002 are culled. In the UK, special rules, which have been discussed elsewhere, are applied.

In addition, the offspring of female BSE cases born during the two years leading up to the BSE diagnosis are culled in most countries in Europe.

**Discussion of the on-farm measures**

The culling approach used can influence motivation to report suspected cases, reducing the willingness of farmers to report suspects, in particular if the need to cull the animals is not evident to the farmer. This effect can be expected to be greater if the impact on the given herd is relatively severe. A herd-culling policy can therefore be assumed to be a greater disincentive. On the other hand, culling only parts of the herds could be economically problematical for some farmers, e.g. if the industry stops taking milk or meat – although considered to be safe (75, 80) – from herds where BSE has occurred. The approach adopted is therefore not only dependent on science; social, political, economic or trading factors also have to be taken into account. In the meantime, birth cohort-culling seems to be the preferred approach in Europe.

**Public health measures**

Until the occurrence of BSE in cattle, no zoonotic potential was known to exist between animal TSEs and human TSEs of any kind. Although no evidence of a link between BSE in cattle and a human TSE was provided before 1996, the theoretical risk had already been discussed in the late 1980s and early 1990s (52).

Since the occurrence of cases of variant Creutzfeldt-Jakob disease (vCJD) (99), BSE has been assumed to be transmissible to humans, but many questions still remain to be answered (70, 72), as follows:

- the species barrier for animal-to-human transmission could be high or low, the magnitude is unknown. Current estimates vary from no species barrier to a factor of 100,000, meaning
that 100,000 times more BSE-contaminated bovine material would be required to infect a human than for bovine-to-bovine transmission – no information is available on a possible threshold dose or the effect of repeated and very low doses of the BSE agent on human health
– the length of the incubation period of vCJD is not known. Hypotheses vary from a few years to more than 25 years – the influence of predisposing factors is not known. Genetic background is an important cofactor. To date, only patients homozygous for methionine/methionine at codon 129 of the prion protein (PrP) gene have developed vCJD. However, this does not preclude that individuals with other genotypes at codon 129 will not develop the disease in the future.
– distribution of infectivity in the various tissues of an infected animal is not fully known. However, most infectivity (about 95%) is found in the brain, the spinal cord and the trigeminal and dorsal root ganglia. The distal ileum also carries a measurable degree of infectivity.

Despite this lack of knowledge, the measures accepted to protect the consumer are described below.

**Ban on specified risk materials in the human food chain**
Excluding SRM from the human food chain effectively minimises the risk of human exposure (69) and is the most important measure taken to protect consumers. Failure to remove SRM would probably expose a large number of consumers to an unnecessary risk.

Muscle tissue has never been found to be infective, even from BSE-affected cattle in the later stages of infection. Furthermore, currently available experimental data strongly suggest that no infectivity is associated with the lymph nodes and spleen of orally infected cattle (77).

**Ban on specified risk materials in the human food chain implemented in Europe**
At the end of 1989, Great Britain (GB) banned the use of SRM for human consumption, namely the brain, spinal cord, tonsils, thymus, spleen and intestines from cattle older than six months. This ban was extended in November 1994 to include the intestines and thymus of animals under 6 months of age. In 1996, meat from most cattle aged over 30 months at slaughter was banned from being sold for human consumption (over-thirty-month rule) (5).

After detection of the first case of BSE in Switzerland, SRM measures similar to those taken in the UK were implemented. All other countries in Europe which reported cases of BSE in the early 1990s only implemented the SRM ban for humans in 1996/1997.

European Union-wide rules banning the use of SRM in the food chain were implemented in October 2000 (28) and amended in 2000 and 2001 (30, 32, 33, 34) to include the intestines of bovines of all ages and the vertebral column from bovines over 12 months of age. The tissues included in the list of SRM vary in the different countries (Table IV). Nevertheless, tissue known to harbour potential infectivity can be found on the SRM list of all the countries in Europe.

**Table IV**
Current list of specified risk materials and date of implementation of the first specified risk materials ban in the human food chain in several countries of Europe

<table>
<thead>
<tr>
<th>Specified risk materials ban</th>
<th>European Union</th>
<th>Great Britain</th>
<th>Portugal</th>
<th>Ireland</th>
<th>France</th>
<th>Switzerland</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bovine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– scull including brain and eyes</td>
<td>&gt;12 months</td>
<td>&gt;6 months</td>
<td>&gt;6 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;6 months</td>
</tr>
<tr>
<td>– tonsils</td>
<td>&gt;12 months</td>
<td>&gt;6 months</td>
<td>&gt;6 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;6 months</td>
</tr>
<tr>
<td>– spinal cord</td>
<td>&gt;12 months</td>
<td>&gt;6 months</td>
<td>&gt;6 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;6 months</td>
</tr>
<tr>
<td>– vertebral column (spinal ganglia)</td>
<td>&gt;12 months</td>
<td>&gt;30 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;30 months</td>
</tr>
<tr>
<td>– intestines (ileum)</td>
<td>all ages</td>
<td>all ages</td>
<td>all ages</td>
<td>all ages</td>
<td>all ages</td>
<td>&gt;6 months</td>
</tr>
<tr>
<td>– mesenterium</td>
<td>all ages</td>
<td>all ages</td>
<td>all ages</td>
<td>all ages</td>
<td>all ages</td>
<td>&gt;6 months</td>
</tr>
<tr>
<td>– spleen</td>
<td>no</td>
<td>&gt;6 months</td>
<td>&gt;6 months</td>
<td>no</td>
<td>no</td>
<td>&gt;6 months</td>
</tr>
<tr>
<td>– thymus</td>
<td>no</td>
<td>&gt;6 months</td>
<td>&gt;6 months</td>
<td>no</td>
<td>no</td>
<td>&gt;6 months</td>
</tr>
<tr>
<td>– visible lymph and nervous tissue</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>all ages</td>
<td></td>
</tr>
<tr>
<td><strong>Ovine and caprine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– scull including brain and eyes</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
</tr>
<tr>
<td>– tonsils</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
</tr>
<tr>
<td>– spinal cord</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
<td>&gt;12 months</td>
</tr>
<tr>
<td>– spleen</td>
<td>all ages</td>
<td>all ages</td>
<td>all ages</td>
<td>all ages</td>
<td>all ages</td>
<td>all ages</td>
</tr>
<tr>
<td><strong>Date of implementation of the mechanically recovered meat (MMR) ban</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
All SRM has to be removed at the slaughterhouses, except vertebral columns, which can be removed at the cutting plants.

Ban on mechanically recovered meat in the food chain
Mechanically recovered meat (MRM) is a type of paste derived from compressed carcasses from which all other consumable tissues have been manually removed. The carcasses include, among others, bones and the vertebral column with the spinal cord and dorsal root ganglia. Mechanically recovered meat is used in cooked meat products, such as sausages and meat pies and is regarded as a major risk factor.

Ban on mechanically recovered meat implemented in Europe
In the UK, bovine skulls and vertebral columns were prohibited from inclusion in MRM in December 1995. The EU banned the use of bones of the head and vertebral columns of bovines for the production of MRM in 2000 (28). This ban was extended to all bones of bovine, caprine and ovine species in 2001 (Table IV) (32).

Bovine spongiform encephalopathy detection at slaughter
Measures for minimising risks for human health require the identification and elimination of infected animals before slaughter, which can only be achieved by a combination of efficient passive and active surveillance. To achieve this goal, extensive information on BSE signs and intensive ante-mortem inspection of adult cattle are required. In cases where animals with clear clinical symptoms are not reported, a penalty should be considered. The testing of cattle at slaughter using the rapid test is no substitute for other public health measures.

Since 2001, several countries in Europe perform blanket testing of all cattle over 30 months of age or even younger. Whether this action offers a measurable increase in safety for the consumer or whether it is more a measure to restore consumer confidence is questionable. Testing of all normally slaughtered cattle has the beneficial effect of removing late preclinical cases from the food chain. However, none of the currently available tests are sufficiently sensitive to identify animals which are infected but do not yet have a high concentration of the BSE agent in the brain. Moreover, all SRM known to harbour potential infectivity have to be removed from the food chain. Additionally, the testing of slaughter cattle can be counter-productive because, due to the perceived total reliability of the testing, other measures such as ante-mortem inspection and SRM-removal are not sufficiently emphasised and implemented. If an individual animal is tested and found to be negative, this should therefore not be considered a guarantee of the absence of the BSE agent (70).

Discussion of the public health measures
The UK and Switzerland implemented the single most important public health protection measure, i.e. the SRM ban in food, at a relatively early stage. In all other countries in Europe, SRM was excluded from the human food chain at a surprisingly late stage, even in countries with reported cases of BSE.

As early as 1992 (62), it was stated that countries could consider supplementary measures ‘which while not fully justifiable on scientific grounds should provide extra guarantees to the consumers’. However, most countries did not apply this recommendation until the announcement of a possible link between BSE and vCJD in 1996. Thereupon, countries with reported cases of BSE implemented the SRM ban. However, the proposal of the EU to ban SRM in 1997 (22) never entered into force. The proposal was modified and only implemented in 2000. Specified risk materials and MRM were therefore only banned in October 2000. This delay of three years before implementation exposed consumers to an unnecessary risk, the consequences of which are impossible to judge as yet.

Today, the most important measures to protect the consumer have been taken. Currently, monitoring the implementation of these measures is important. A test has been developed in which central nervous tissue can be detected (56) to prove the absence of SRM in meat products. Apart from this laboratory test, inspections at the slaughterhouse and cutting-plant level should also be tightened to guarantee compliance with the SRM and MRM bans.

Import measures
The agreement on the application of Sanitary and Phyto-sanitary measures (SPS Agreement) encourages World Trade Organization (WTO) members to base their measures on international standards, guidelines and recommendations. The relevant international standard for animal health and zoonoses is the International Animal Health Code (the Code) (65). A higher level of protection can be chosen if there are scientific grounds for doing so (84). This should be conducted on the basis of an import risk assessment. The principal aim of import risk analysis is to provide importing countries with an objective and defensible method of assessing the disease risks associated with the importation of animals and animal products. The analysis should be transparent so that the exporting country is provided with clear reasons for the imposition of any import conditions or refusal to import. A reasoned relationship must exist between the measures chosen and the risk assessment, so that the results of the risk assessment support the measures. Where significant uncertainty prevails, a precautionary approach may be adopted. However, the measures selected must nevertheless be based on a risk assessment that takes account of the available scientific information. Simply concluding that measures will be selected on the basis of a precautionary approach because
significant uncertainty exists is unacceptable. The rationale for selecting measures must be made apparent (59).

The best means of preventing the introduction of BSE is to control the import practices for certain products from countries with BSE and with the risk of having BSE. The main risks for the cattle population arise from the importation of live cattle or of feedstuff containing MBM from ruminants. One of the major problems encountered is that neither live cattle nor MBM can be tested for BSE infectivity. Detection of cases of preclinical BSE is impossible with currently available test methods. Quarantine measures are also not appropriate because of the long incubation period of approximately five years. Avoiding imports of infectious material is therefore only possible through stringent import restrictions based on risk assessment.

Current recommendations of the Office International des Épizooties

The OIE International Committee was first informed of BSE in 1988 (60). A special expert meeting on BSE was held in September 1990 (61). The OIE issued the first recommendations on BSE in the Code at the General Session of the International Committee in 1992. The BSE chapter in the Code has since been continuously amended. Some of the main recommendations of the current Code (65) are summarised below.

Regardless of the BSE status of the exporting country, the trade of some commodities, such as milk and milk products, semen and embryos, hides and skins should be authorised without restriction.

Ruminant-derived MBM or commodities containing such products from countries with minimal, moderate or high risk of BSE should not be traded between countries. The following procedure should be used for the inactivation of TSE agents for the production of MBM containing ruminant proteins: the raw material should be reduced to a maximum particle size of 50 mm before heating, the raw material should be heated under saturated steam conditions to a temperature of not less than 133°C for a minimum of 20 min at an absolute pressure of 3 bar (Appendix 3.6.3. of the Code).

The recommendations concerning imports of cattle are adapted according to risk status. The main recommendations for cattle selected for export from countries with a risk of BSE are that they be sufficiently identified and are not the offspring of suspected cases. In addition, the cattle must be born after the date from which the ban on the feeding of ruminants with MBM derived from ruminants came into force. For countries that are free or provisionally free of BSE, the recommendations are less stringent.

For the import of meat and meat products from cattle, it is recommended that, in the exporting country, the feeding of ruminants with MBM derived from ruminants be banned and the ban must be effectively enforced. Furthermore, an ante-mortem inspection is recommended. Inclusion of or contamination with SRM and MRM has to be excluded, except for imports from BSE-free countries. The list of SRM varies according to the BSE status of the various countries.

Import measures implemented in Europe

In 1989, the EU banned the export from the UK of cattle born before 1988. With the introduction of the SRM ban in the UK, the EU (16) restricted imports of live cattle to young calves, which have to be slaughtered by 6 months of age. This amendment should avoid the problem of importing countries having to remove and dispose of SRM from cattle imported from the UK.

In 1990, the UK banned the export of SRM and feed containing SRM. The EU did not ban the import of mammalian MBM from the UK until 1996 (19).

In March 1996, the EU banned the export of all cattle and cattle products from the UK, except milk and semen (19), although the ban was later partly lifted (23, 25).

In 1996, some member countries implemented bilateral import restrictions against countries in which BSE had been reported. These bilateral import measures were, in most cases, very extreme and included a ban on nearly all bovine material, in some cases including bovine semen. However, the restrictions for trade within the EU were mainly not affected.

Until 2001, no trade restrictions concerning live animals, products thereof and MBM between member countries had been implemented by the EU except for Portugal (24) and the UK.

Import conditions for ruminants and ruminant-derived products have only recently been completely revised. In future, imports should be restricted according to the risk status of each country, which has yet to be established (35). Until the BSE status of the country is established, transitional measures apply (37). Import conditions are very detailed and extensive and transitional measures will be replaced in the near future. Only the central points of the future conditions are therefore mentioned below, as follows:

– imports of cattle from BSE-risk countries is only possible if the feeding of MBM to ruminants has been banned and is effectively enforced. The cattle for export should either be born after an effective feed ban or originate from herds having reported no BSE cases for seven years
– the conditions for imports of meat and meat products of bovine origin are similar to the OIE recommendations. The central point is that the feeding of ruminants with MBM has been banned and the ban has been effectively enforced in the
exporting country. Specified risk materials and MRM must be
excluded from meat products. Exceptions are foreseen for
countries proven to be free from BSE.

Discussion of the import measures

The late introduction of the ban on MBM exports facilitated the
spread of contaminated MBM all over Europe and from there,
to other parts of the world. Although no formal import ban was
implemented by the EU before 1996 (19), exports from the UK
to the EU decreased. In 1994, the feeding of MBM to ruminants
was banned in all EU countries. As a result of this ban, and
especially since the beginning of the 1990s, MBM was exported
from the UK to countries outside the EU (1). Available
import/export statistics have to be evaluated carefully because
they do not allow a distinction to be drawn between different
forms of processed animal proteins, either by type of product or
by species from which they are produced.

The export figures of MBM from EU member states show that
exports of MBM, especially into countries in eastern Europe,
increased sharply in the early 1990s (Fig. 3). In particular,
MBM exports from, at that time, ‘BSE free-countries’ contained
SRM and were, in most cases, not heat-treated with the
rendering parameters of 133°C at a pressure of 3 bar for
20 min, before 1997. Most countries in eastern Europe had not
implemented sufficient measures at the time of importation to
avoid recycling of the BSE agent. These imports therefore posed
a significant risk of introducing the BSE agent into the cattle
populations of countries in eastern Europe (Fig. 3).

In Europe, trading of MBM is now only possible for use in pet
food, for fur animals and for destruction. Other imports of
animal protein meal consist of fish and poultry meal. Experience shows that this meal could be contaminated with
ruminant MBM and therefore all animal-derived meal should
be controlled for inclusion of ruminant MBM at import.

Although the possibility was acknowledged that some infected
cattle could be imported from the UK, the statistical probability
– unless large numbers of cattle were imported – was judged to
be relatively small. After the implementation of the EU ban on
exports from the UK of cattle born before 1988, the risk from
cattle born after the feed ban was assumed to be zero’ (52).

With the reporting of BSE cases in other countries, no other
substantial restrictions were imposed until 1996. Only when
the possible link between BSE and vCJD was made public in
March 1996 (99), was a wide range of import restrictions
introduced against countries where BSE had been reported.
Surprisingly, intra-community trade remained more or less
unaffected and millions of cattle from BSE-affected countries
were imported to other EU member states without restrictions.

The current trade restrictions of the EU are still debatable.
Cattle can be traded after the implementation of an ‘effective
feed ban’. This means that theoretically, only cattle born after
the total feed ban should be traded. Although EU guidelines
with regard to effective feed bans exist (39), the ‘effective feed
ban’ is still not defined. Trade of cattle, including animals born
before the SRM ban in feed and implementation of the total
feed ban, is still ongoing, partly into countries in Europe with
no consumer protection measures, such as the SRM ban.

Additionally, MBM can still be traded for use in pet food,
provided that SRM is excluded. However, the rendering
parameters of 133°C at a pressure of 3 bar for 20 min are not
imposed by law, although these conditions are apparently taken
into account in the certificates for imports into the EU.

In summary, most of the import restrictions implemented have
been as follows:

– too late in view of the fact that, by the time BSE cases were
  recognised, infected cattle and MBM had already been exported
  for many years

– only directed at countries with reported cases, so countries
  with a poor surveillance system were encouraged to export as
  this was still possible under the cover of BSE-freedom; these
  countries also had no measures in place, so the import risk from
  these countries was probably greater than from countries
  known to have BSE

– based neither on OIE recommendations nor on risk
  assessment.

On the other hand, import measures were frequently extremely
harsh and included commodities which are considered to be
safe, such as semen and milk, and in most cases, not based on
scientific findings but defined as a ‘precautionary approach’.
Unjustified import measures were often discontinued after the
occurrence of the first BSE case in the country concerned.
Risk management of transmissible spongiform encephalopathy in small ruminants in Europe

**Surveillance**

Although scrapie is a notifiable disease, experts suspect that the incidence of the disease is under-reported. Estimates from EU member states suggest that scrapie prevalence in adult sheep could range from 20 to 500 positive animals per 1 million adult sheep. Underestimation levels of between 30% and 87% have been reported for scrapie (51). Given the impossibility of discriminating between scrapie and BSE in sheep, either clinically or pathologically, the following text refers to 'TSE in small ruminants'.

The current OIE Manual of Standards for Diagnostic Tests and Vaccines does not contain diagnostic procedures for TSE in small ruminants. However, as with BSE, the diagnostic procedures used are histopathology and immuno-histochemistry. No rapid tests have yet been validated, but given the similarity of the brain matrices and the non-specificity of the antibodies used, it is anticipated that the rapid tests used for BSE in cattle will also be effective for detection of the TSE agent in small ruminants (81). Tests for use in tissues that show infectivity in the early stages of incubation, such as lymphoid tissue, are still being developed and will probably not be available for routine applications before a while (82). The only method currently available to differentiate between scrapie and BSE in small ruminants is a comparative assessment of incubation time and pathological lesion profiles in the brains of mice inoculated with the isolates (8). Several other methods have been developed, but none have been validated (81).

With regard to TSE in small ruminants, active surveillance using the BSE rapid test has been mandatory since April 2002 (40). Up until the present, more than 500,000 tests have been required across the EU, although some member states are considering testing larger numbers of animals. Surveillance will concentrate on healthy stock, fallen stock and clinically suspect animals over the age of 18 months. All positive animals should be examined using a method that discriminates between scrapie and BSE in small ruminants (81). First results reveal that there is significant under-reporting of TSE in sheep and goats (42).

**Animal health measures**

Notwithstanding the absence of evidence that BSE exists in sheep under natural conditions, many of the animal health measures which apply to BSE in bovines also apply to small ruminants. The feed bans of MBM were, in most cases, not restricted to cattle, but applied to all ruminants. Furthermore, the process parameters for treating animal waste should have an effect for small ruminants. Except in the UK, SRM from sheep and goats was only excluded from the feed chain in October 2000.

Currently, it cannot be judged whether these measures have been effective in minimising the risk of recycling the TSE agent in small ruminants, mainly because surveillance in small ruminants has been insufficient.

**On-farm measures**

Given the transmissibility of scrapie infection within a flock and between flocks by direct or indirect contacts, elimination of the index case alone will not eliminate the enhanced risk in a flock of small ruminants in which a TSE case has been confirmed. A culling strategy which covers the entire flock where the index case was found should therefore ideally be applied, and possibly extended to those flocks which had been in contact with the original flock or the index case. However, the culling strategy has to be modified for the different genotypes (82).

Several scenarios have been tried in a number of countries, but the ideal approach has yet to be found. The tested measures include total flock depopulation, partial flock depopulation (high-risk animals, bloodline animals, etc.) or removal of only those animals affected with scrapie. Another approach being taken by countries or regions within countries is to breed the more ‘resistant’ genotypes.

European Union legislation requires that sheep and goats, which are confirmed to have scrapie, must be disposed of (35). Moreover, in most member states, all other small ruminants on the same holding and the offspring of the affected animal are destroyed.

**Public health measures**

Given the wide distribution of TSE infectivity in sheep tissues, exclusion of SRM is much more difficult (82). Unlike the situation in experimentally-infected cattle, the distribution of infectivity in experimentally-infected sheep tissues at different time intervals, resulting from exposure by the oral route to a large dose of the BSE agent, indicates widespread involvement of lymphoid tissue at an early stage of the incubation period. Only some months after exposure to the BSE agent, susceptible sheep show an estimated significant load of BSE infectivity in the intestines, lymph nodes, tonsils, stomach and spleen. The pathogen load in the intestines of BSE-infected small ruminants is higher than that in the central nervous system tissue at the beginning of the incubation period and of the same order of magnitude toward the end of incubation. However, distribution of infectivity seems to be different for certain genotypes; in semi-resistant genotypes, infectivity seems to be restricted to the central nervous system (82).
The heads of sheep and goats were banned in the UK after detection of infectivity in the spleens and brains of sheep experimentally infected with BSE (44). Specified risk material from sheep and goats was also banned in the EU in October 2000 (Table IV).

The exclusion of other tissues such as the intestines is already under consideration. Should BSE be found in sheep in the field, the list of SRM in the future will be very different from the current list.

General conclusions

Most countries in Europe did not introduce adequate measures to combat BSE until cases had been reported in their country. As the label ‘no BSE cases detected’ was equated with ‘BSE-free’, the prophylactic measures to protect the consumer, i.e. removal of SRM, were, in particular, not contemplated and generally considered to be exaggerated.

Experience in Europe shows that there is no definitive concept for combating BSE. Measures taken have to be assessed, then continuously modified and adapted to the situation in the country. There are several possible ways of achieving the objective, depending on circumstances, but what is required above all is a combined set of complementary measures.

The next challenge is BSE in small ruminants. The answer to the question whether lessons have been learned from the history of BSE in cattle is partly yes, because some risk-reducing measures have already been implemented without knowing whether the disease exists. However, it is generally accepted that these measures will be insufficient if BSE in small ruminants is confirmed. The theoretical nature of the risk makes judging the proportionality of the control measures particularly difficult. Whilst there is a theoretical risk of exposing the human population to a continuing source of BSE, there is also a risk of inflicting serious damage to the communities involved in the sheep industry if BSE is ultimately never found to be present in small ruminants in the field (2).

The history of this disease shows the difficulty of managing a disease that is fraught with so many unknown factors. If a risk assessment has to be undertaken on the basis of assumptions rather than facts, the outcome is questionable. Concluding that there is a possibility of a risk arising is not sufficient. An evaluation of the likelihood of the risk must be undertaken and the risk evaluated must be ascertainable. Basing policy decisions on such risk assessment is difficult. Notwithstanding these difficulties, action must be taken. A degree of uncertainty will always persist as there is no such thing as zero risk. Stating that ‘everything that can be done is being done’ is illusionary. If the principle of full precautions were adopted in the case of TSE, the agricultural industry of Europe would probably collapse (26). Concisely, defining an acceptable level of risk is an important requirement.

The most important measures to combat BSE and to protect the consumer have now been implemented in the EU and in most countries in Europe having reported BSE cases. However, some countries in Europe without reported cases of BSE have still not implemented adequate measures, even though they are assessed to be at risk of being affected by BSE (73, 78).

However, there is no point in proposing regulations if they are not implemented. National supervisory teams should therefore regularly evaluate implementation procedures. Such enforcement teams have been in place for a few years in the UK and Switzerland. Results so far confirm the need for establishing units which ‘control the controllers’. Correct and impeccable application of the various measures is crucial for safe food and essential to regain consumer confidence in food originating from animals.

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La gestion des risques posés par les encéphalopathies subaiguës spongiformes transmissibles en Europe

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Résumé
C’est en novembre 1986 que l’encéphalopathie spongiforme bovine (ESB) a été décrite pour la première fois au Royaume-Uni. La mise en place d’un système de surveillance active s’est accompagnée de la déclaration obligatoire des cas d’ESB dans le cheptel bovin de la plupart des pays européens, illustrant ainsi l’importance d’une utilisation combinée de dispositifs de surveillance active et passive pour apprécier le statut réel de l’ESB dans un pays donné.

La tremblante, une encéphalopathie subaiguë spongiforme transmissible (ESST) présente chez les ovins et caprins, a été signalée dans le monde entier, à quelques notables exceptions près. On s’est également inquiété de la contamination possible des ovins et des caprins par l’ESB. Actuellement, chez les petits ruminants, la tremblante ne peut être distinguée de l’ESB qu’à l’issue de longues expérimentations sur les souris. Les premiers résultats de la surveillance active de la tremblante commencée en 2002 ont révélé que le nombre de cas signalés avait été largement sous-estimé.

L’histoire de l’ESB chez les bovins révèle que les pouvoirs publics ont pris des décisions inappropriées en termes de gestion des risques, faute d’avoir tenu compte du risque identifié par les analyses de risques dans un pays donné. Aucune mesure de protection de la santé animale et de la santé publique n’a été mise en place malgré la probabilité de ce risque. Par ailleurs, l’impact des mesures adoptées a souvent été surestimé, et il a fallu les revoir à plusieurs reprises.

L’interdiction de la farine de viande et d’os (FVO) dans les aliments pour ruminants est la principale action destinée à prévenir l’apparition de nouveaux cas d’ESST. En outre, il convient d’étudier des mesures complémentaires, telles que l’exclusion des matières à risque spécifiées et des cadavres issus de l’équarrissage, ainsi que la prévention de contamination croisée entre les aliments pour animaux et la FVO. L’interdiction des matières à risque spécifiées (encéphale et moelle épiplène, par exemple) susceptibles de contenir des agents de l’ESB en forte concentration, ainsi que l’interdiction de la viande séparée mécaniquement des os, sont les mesures les plus importantes en vue d’assurer la protection du consommateur.

Les principaux moyens mis en œuvre en Europe ainsi que leur justification scientifique sont décrits et discutés.

Mots-clés
Gestión del riesgo de encefalopatías espongiformes transmisibles en Europa

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Resumen
La encefalopatía espongiforme bovina (EEB) fue descrita por primera vez en el Reino Unido, en noviembre de 1986. Tras la introducción de un sistema de vigilancia activa, la mayoríá de los países de Europa han señalado casos de EEB en sus poblaciones bovinas, lo que pone de manifiesto la necesidad de proceder a una vigilancia activa además de la vigilancia pasiva para evaluar la verdadera situación de un país respecto de la EEB.

El prurigo lumbar es una encefalopatía espongiforme transmisible (EET) de ovinos y caprinos señalada en casi todos los países del mundo. Se teme que la EEB haya sido introducida en el ganado ovino y caprino. En la actualidad, la distinción entre el prurigo lumbar y la EEB en pequeños rumiantes sólo es posible mediante largos experimentos en ratones. Los primeros resultados de la vigilancia activa, introducida en 2002, revelan que el número de casos declarados es muy inferior a la realidad.

La historia de la EEB en el ganado bovino demuestra que las evaluaciones de riesgo fueron a menudo ignoradas en determinados países y, por consiguiente, se adoptaron decisiones inadecuadas en materia de gestión del riesgo, es decir que aunque existía probabilidad de riesgo no se tomaron las medidas zoosanitarias y de salud pública adecuadas. También se sobrestimó con frecuencia el efecto de las medidas adoptadas y hubo que corregirlas en repetidas ocasiones.

La principal medida para evitar nuevos casos de EET es la prohibición de alimentar a los rumiantes con harinas de carne y huesos. Otras medidas que deben contemplarse son la exclusión de las materias específicas de riesgo y canales de las operaciones de procesamiento, la definición de parámetros para los sistemas de procesamiento de desperdicios de matadero y la prevención de la contaminación cruzada de los alimentos para animales con harinas de carne y huesos. Las principales medidas para proteger al consumidor son la prohibición de introducir en la cadena alimentaria materias específicas de riesgo, como el encéfalo o la médula espinal, que pueden contener concentraciones particularmente altas del agente de la EEB, y la prohibición de introducir en la cadena alimentaria carne separada por procedimientos mecánicos.

Los autores describen y comentan las principales medidas adoptadas en Europa y los criterios científicos en que se basan.

Palabras clave
References


