THE FUTURE OF BSE FROM THE GLOBAL PERSPECTIVE

D. Heim*, L.Mumford

*Corresponding author: Swiss Federal Veterinary Office, e-mail: Dagmar.Heim@bvet.admin.ch

Abstract

Although the BSE risk of most countries in Europe has been assessed and they have implemented both measures to control BSE and extensive surveillance systems, complete and valid data is still not consistently available. Globally, data is largely unavailable. Assessments based on incomplete or invalid information could lead to false conclusions. The BSE risk of countries throughout the world must continue to be assessed, and improvements in collection of surveillance data must be made, both in countries already reporting BSE cases and worldwide, in order to evaluate the global BSE picture and assure that cattle and products can be safely traded.

*Keywords**:** BSE, surveillance, risk assessment, GBR*

BSE in the world: what we know today

After bovine spongiform encephalopathy (BSE) was first diagnosed in cattle in the United Kingdom (UK) in 1986 (Wells et al., 1987), it became clear that the disease had been spread throughout Europe through trade in live animals, meat and bone meal (MBM) contaminated with the BSE agent, and feeds containing this MBM. Now, it is evident that the disease agent has continued to spread throughout the world through global trade in these products (Figure 1).

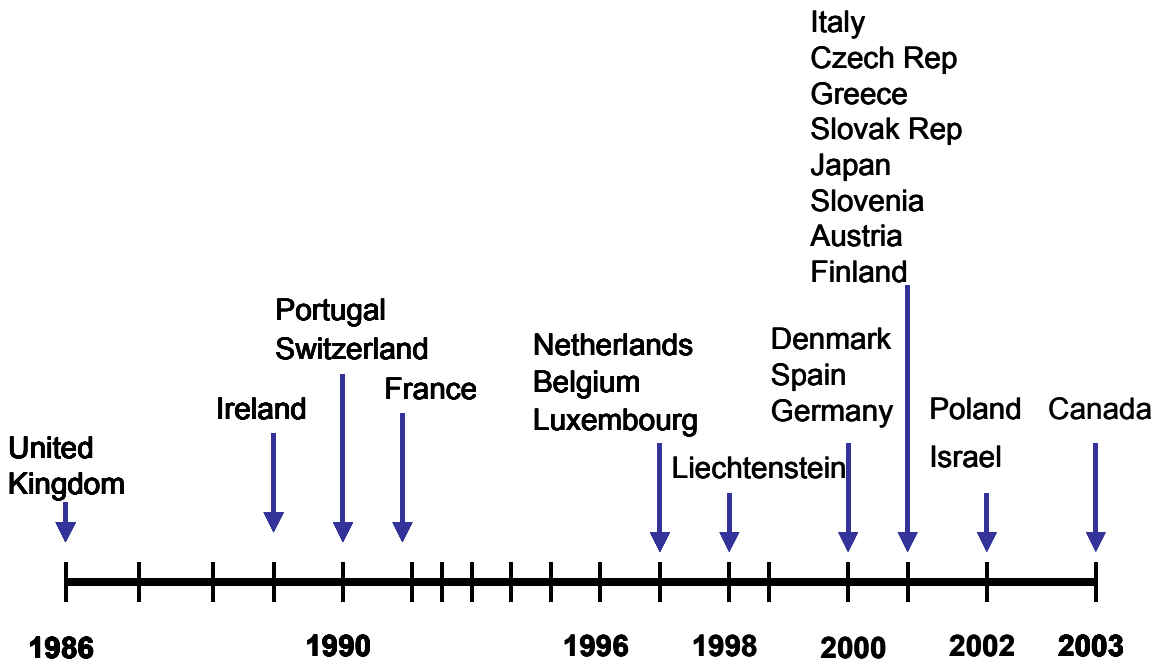

Figure 1: Year of first reporting of indigenous BSE cases

Extensive epidemiological studies have traced the cause of BSE to animal feed containing inadequately treated ruminant MBM (Wilesmith, Wells, Cranwell & Ryan, 1988), which was then recycled through the rendering/animal feed chain and amplified over time. It is possible that this amplification cycle began in the UK as early as the 1970s (Wilesmith, Ryan & Atkinson, 1991). The appearance of indigenous BSE cases throughout the world (e.g. Japan in 2001, Israel in 2002, North America in 2003) (Office International des Epizooties, 2004c) shows that, once the BSE agent is introduced, this cycle can be propagated outside Europe.

However, it was only after implementation of active surveillance programs targeted to BSE risk populations that many countries (in Europe and elsewhere) finally detected BSE, and year after year more countries detect their first BSE cases. Most of these countries had previously considered themselves to be “BSE-free” and many had exported BSE risk products. Trade in these products still continues among some countries that are considered “BSE-free” but possibly could have undetected cases. Therefore it is essential to be able to determine if an exporting country could have BSE before the first case is detected.

Risk Assessment & the GBR

This determination of the BSE status of a country can only be made on the basis of the outcome of a BSE risk assessment, which evaluates imports, surveillance data, and internal factors. This recommendation is codified in the BSE chapter of the Terrestrial Animal Health Code of the World Organisation for Animal Health (Office International des Epizooties, 2004a).

On the basis of the recommendation of the OIE, the Scientific Steering Committee (SSC) of the European Commission initiated the "Geographical BSE Risk Assessment" (GBR) for several countries. The GBR is defined as a qualitative indicator of the likelihood of the presence of one or more cattle being infected with BSE, pre-clinically or clinically, within the native cattle population of a country at any given point in time. In countries already reporting BSE, the GBR gives an indication of the level of infection (Scientific Steering Committee, 2000a, Scientific Steering Committee, 2000b, Scientific Steering Committee, 2002a, Scientific Steering Committee, 2002b, Scientific Steering Committee, 2002c).

The GBR qualitatively assesses risk factors that contribute either to the potential for introduction of BSE into the country or to the ability to cope with an introduction by asking the following questions:

- Had the agent been introduced to the country by import of potentially infected cattle or by feed with MBM, and if so to what extent ("external challenge")?

  In the assessment it is assumed that the BSE agent can only be introduced into a country by imports of cattle and MBM.

- What would happen if the agent were introduced into the animal production system, i.e. would it be amplified or eliminated ("stability of the system")?

  When risky imports are found to have occurred, the system's ability to minimize the exposure of cattle is evaluated in terms of the use made of MBM, the use made of SRM, the rendering conditions, and the feeding systems.

Currently 63 countries have been assessed (Table 1). These countries have been categorized into the following four levels defined by the SSC:

GBR I: highly unlikely that any BSE infected cattle are present.

GBR II: the presence of any BSE infected cattle is still unlikely, but it cannot be excluded.

GBR III: the presence of BSE infected cattle is likely or, if cases already were discovered, the number of BSE cases identified during the last 12 months is below 100 per million adult cattle.

GBR IV: more than 100 BSE cases per million adult cattle were discovered in the last 12 months.

The GBR has proven to be a useful tool in assessing countries in terms of their potential BSE risk. Before the detection of the first cases in many "BSE free" countries, the GBR showed that a risk could be present by categorizing them as GBR III. For example, Germany, Italy, Spain, the Czech Republic, the Slovak Republic and Poland, none of which had reported indigenous cases of BSE at the time of the original assessment, were included in GBR III and subsequently reported BSE in their national herds. Israel detected their first BSE case before the assessment was finalized, but the draft report already indicated GBR III. Thus, the results of the GBR (or any objective, comprehensive risk assessment) can be practically and reliably used to estimate the likelihood of a BSE problem in countries and categorize countries according to their risk.

However, as with all risk assessments, valid data is required to give a valid outcome. Until 2002, the GBR only considered imports of live cattle and MBM from countries with confirmed BSE cases as an external challenge. The subsequent detection of BSE cases in some GBR II countries (e.g. Austria, Finland, Slovenia and Canada) indicated that the approach underestimated the risk. In 2002 the method was changed to consider imports from all GBR III countries as an external challenge, even in the absence of reported cases.

Table 1: GBR level of countries assessed through June 2004

GBR I	Argentina*, Australia, Botswana, Brazil*, Chile*, El Salvador, Iceland, Namibia, New Caledonia*, New Zealand*, Nicaragua, Norway, Panama, Paraguay*, Singapore*, Swaziland, Uruguay*, Vanuatu*
GBR II	Colombia, Costa Rica, India, Kenya, Mauritius, Nigeria, Pakistan, Sweden, USA
GBR III	Albania, Andorra, Austria, Belarus, Belgium, Bulgaria, Croatia, Denmark, Canada, Cyprus, Czech Republic, Estonia, Finland, Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg, Malta, Poland, The Netherlands, Romania, San Marino, Slovak Republic, Slovenia, Spain, Switzerland, Turkey
GBR IV	United Kingdom, Portugal

* Newly assessed in 2002/2003

Therefore, all GBR I and II countries have had to be re-assessed under these criteria. Re-assessments of some countries are complete and some are still ongoing. However, these re-assessments were initiated before the BSE cases in North America were reported and so, again, some re-assessments are necessary to account for this increased risk. This emphasizes the fact that, as the BSE situation changes worldwide, national risk assessments should be updated continuously using the most current data in order to remain valid and useful. As well, the fact that assessments should be carried out for all countries is clearly shown.

Risk assessments can also be used to ask additional questions, such as what are the BSE risk populations within the country, in order to guide development of a surveillance system. Although initial assessments of BSE risk can be performed using challenge data and internal stability data, further assessment requires additional information, such as surveillance data, from within the country, making risk assessment an iterative process.

Surveillance

Surveillance programs for BSE should be determined by, and commensurate with, the outcome of a national BSE risk assessment, as recommended by the Terrestrial Animal Health Code of the OIE (Office International des Epizooties, 2004b). The two major objectives for BSE surveillance are to determine whether BSE is present in the country, and, if present, to monitor the extent and evolution of the prevalence over time, thus monitoring the effectiveness of measures in place. It is important to remember that the number of BSE cases reported by a country can only be evaluated within the context of the quality of the national surveillance system. However, although OIE provides general guidelines, it does not currently provide specific guidelines for an appropriate level of surveillance for the different BSE risk categories. This makes the comparison and evaluation of national surveillance systems even more difficult.

Passive surveillance

Until 1999, BSE surveillance was limited to the notification of clinically suspected cases (passive surveillance). Mandatory reporting is certainly a basic requirement for a surveillance system, and in many countries it was assumed that this level of surveillance would allow early detection of a BSE outbreak.

However, passive surveillance relies solely on the identification and reporting of clinical suspects by farmers, veterinarians and others involved in handling animals to the veterinary authorities. For this system to function effectively, several factors must be considered (Doherr, Heim, Fatzer, Cohen, Vandevelde & Zurbriggen, 2001):

- Disease awareness at every level and in every sector is essential. Cases are often overlooked because the more dramatic clinical signs are normally only observed at the end-stage of the disease. Farmers, veterinarians, slaughterhouse personnel and others handling cattle play a crucial role and should be trained to recognize even the subtle, early signs of BSE. This requires an extended, long-term education program.

- The willingness to report suspected BSE cases is also essential. There must be minimal negative consequences to the identification of a positive case at the farm level, i.e. measures must be "reasonable". The motivation is low for a farmer to notify a suspect case if their whole "life-work" could be destroyed, therefore all consequences should be understood and accepted by the farmers and a reasonable compensation paid. Moreover, the stigma associated with BSE – especially with the first cases of BSE detected – should not be underestimated. These issues can be improved through proactive communication of information.

- Adequate laboratory competence must be available to ensure appropriate handling and examination of brain or other tissues collected through the surveillance system.

Because these factors vary greatly, both among countries and within countries over time, the results of passive BSE surveillance systems are subjective and evaluation and comparison of reported case numbers should be made carefully.

For example, the legal framework for passive surveillance within all EU member countries states that cattle of all age with clinical signs consistent with BSE should be examined for BSE. However, even within this stringent EU framework, variability exists, and some EU countries with a known BSE problem do not test the minimum number of animals set forth in the OIE code (Office International des Epizooties, 2004b). In the OIE code section, the minimum number of animals exhibiting one or more clinical signs of BSE (clinical suspects) that should be tested (based on the total cattle population over 30 months of age) is indicated, and suggestions are that the number is even too low. However, analysis of the number of tests performed in the EU between 2001 and 2003 showed that the number of suspect cattle examined varied between 2 and 408 per million adult cattle. (European Commission, 2002, European Commission, 2003, European Commission, 2004). Therefore, despite the OIE code recommendations, much less the stringent EU regulations, in some member states passive surveillance seems to be nonexistent and, with a few exceptions, it may be actually declining (Table 2).

Given this variability in the factors involved and the difficulty in effectively implementing a passive system, it has become obvious that passive surveillance alone is not sufficient to establish the real BSE status of a country, therefore, other solutions were sought.

Active surveillance

Other groups of cattle that are at increased risk of having BSE have been identified and can be actively targeted within a national surveillance system to improve the chances of identifying positive animals in the overall population and improve the validity of the data. These risk groups include cattle with signs of disease non specific to BSE (e.g. weight loss, loss of production) and cattle that died or were killed for unknown reasons. In different countries these animals may be defined as sick slaughter, emergency slaughter, fallen stock, or downer cows. It is known from the pathogenesis of the disease that cattle younger than 30 months rarely test positive, so the age of the population tested also is important.

Table 2: Number of clinically suspected cases of BSE per million adult cattle in the European Union, 2001-2003

Country	Clinical suspects per million cattle		
	2001	**2002**	**2003**
Austria	2	4	2
Italy	3	29	19
Finland	8	15	13
Greece	10	0	3
Germany	32	55	136
Sweden	36	37	23
France	43	18	39
Netherlands	54	23	15
Denmark	81	42	42
Spain	136	20	21
Luxembourg	140	140	40
Ireland	142	142	92
Belgium	161	186	111
UK	228	174	91
Portugal	408	188	128

For example, in January 1999 Switzerland initiated an active, targeted surveillance scheme to enhance the detection of BSE cases in the adult cattle population (Doherr, Oesch, Moser, Vandevelde & Heim, 1999). In addition to the mandatory reporting of all suspect clinical cases, all cattle that are in the above groups and that have at least four permanent incisors are tested. Additionally, a random sample of apparently healthy cattle is examined during regular slaughter to minimise diversion of questionable animals to slaughter (i.e. to improve compliance with passive surveillance and reporting). The development of rapid BSE tests (Scientific Steering Committee, 1999, Scientific Steering Committee, 2002d) facilitated testing of the increased number of samples collected through this system.

n the spring of 2000, a similar surveillance approach was introduced in Western France (Calavas et al., 2001). In January 2001, the EU introduced a standard system for the active screening of cattle for BSE (Heim & Kihm, 2003), in which all animals in the entire risk population (i.e. all cattle that have died or been killed on farm or during transport, fallen stock, and cattle sent to emergency/sick slaughter) over 24 months of age are tested. Additionally, all cattle subject to regular slaughter over 30 months of age are tested. Through this program, many more positive cases were detected and the number of reported cases in the EU increased in 2001 and 2002. In the 15 original countries of the EU (EU 15) in 2003 1,364 cattle were positive of more than 10 million tested. This suggests an overall downward trend in the number of cases. Interestingly, Spain and Portugal were the only countries in the EU 15 with increased cases in 2003 (figure 2). The basis for this reported increase is unclear.

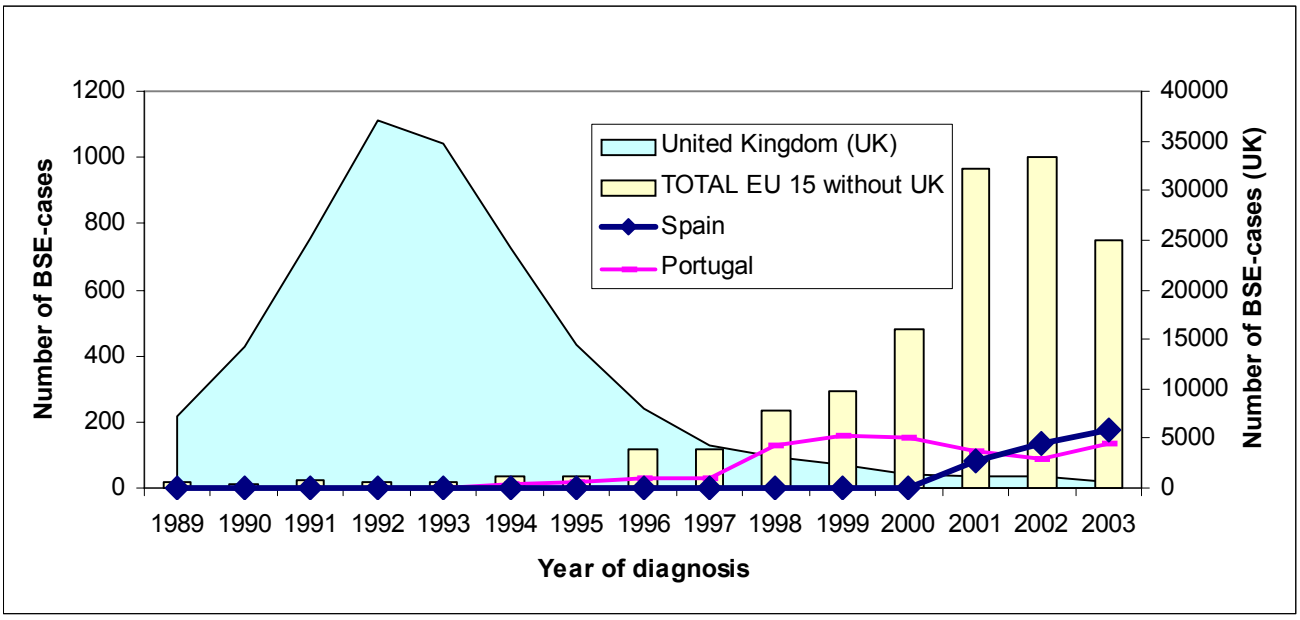

Figure 2: Number of BSE cases in the 15 original member states of the European Union from 1989 to 2003

Despite the fact that all EU member countries have the same legal requirements for surveillance (except UK and Sweden which have special regulations), other variability and inconsistencies can also be identified.

One evaluation of the data from 2001 and 2002 concluded that active BSE surveillance was operating reasonably in most member states although anomalies persisted (Bird, 2003). However, it is clear that some of the countries with a very low number of cases also tested fewer animals (Figure 3 and 4) and that the number of cattle tested varies substantially among member states. For example, the risk population tested has ranged between 0.62% and 5.86%, and the population of cattle at regular slaughter has ranged between 7.5% and 37.9% (excluding UK and Sweden) of the total adult live cattle population. Although some variations in the number of tests performed could be explained by different production and detection systems, the deviation is that significant that it can only be explained with an imperfect implementation of surveillance. This emphasizes that legal requirements alone are not sufficient and enforcement of implementation is crucial.

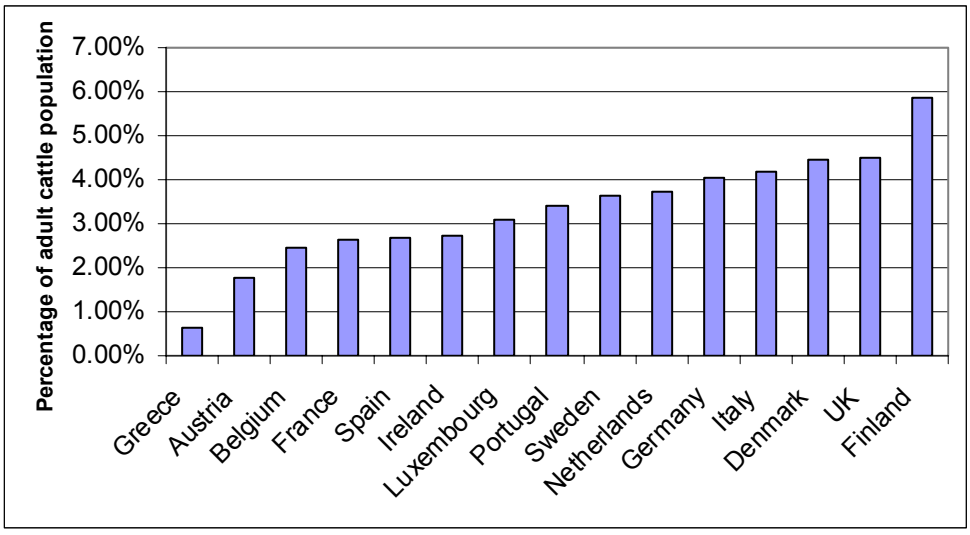

Figure 3. Cattle tested from the risk population, shown as a percentage of the adult live cattle population

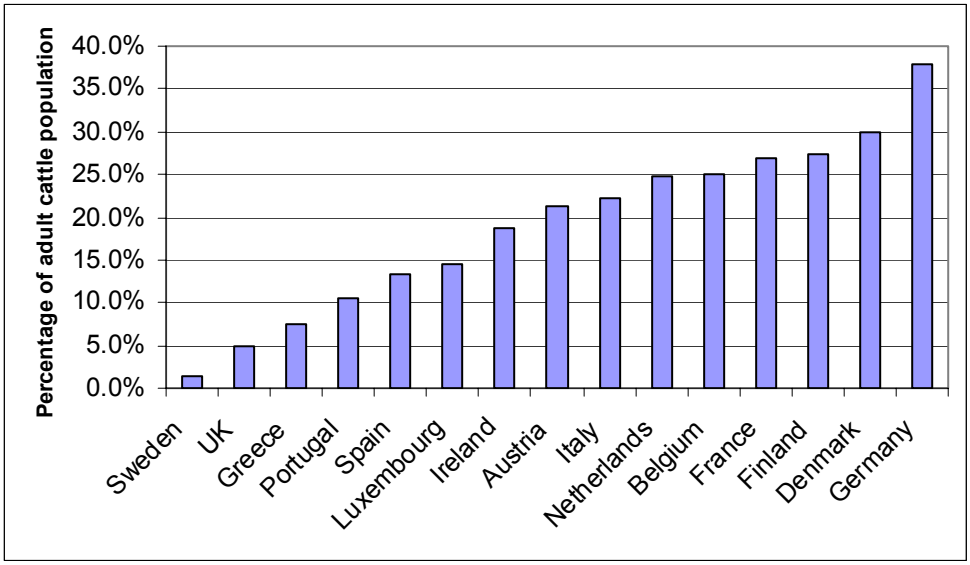

Figure 4. Cattle tested from the regular slaughter population, shown as a percentage of the adult live cattle population

The variability in the cattle population tested also affects the interpretation of the results. If risk populations, as described above, are tested, the efficiency of testing (i.e. the number of tests performed to find one positive) increases. If testing focuses on regular slaughter cattle, especially cattle younger than 30 months (or even younger than 24 months), a country may report a very high number of tests performed and low number of cases, but these numbers only give part of the picture. Most reports of tests performed and cases reported are not age adjusted, making country-to-country comparisons difficult. In addition, testing large numbers of low risk animals greatly increases the cost of a surveillance program, which may be especially important for countries with limited resources (Table 3).

Table 3: Number of cattle tested and BSE positive cases in the risk and the regular slaughter populations in the European Union

	Regular slaughter population		**Risk population**	
Year	2002	2003	2002	2003
number of cattle tested	7’511’862	8’716’481	1’030’484	1’295’770
number of BSE positives	237	265	938	783
rate of positives: 1 of	31’696	32’892	1099	1655
Costs to find one positive BSE case (assuming €70/ sample)	**€ 2,2 million**	**€ 2,3 million**	**€ 76901**	**€ 115’841**

Taken together, the different aspects of the variability in implementation make it extremely difficult to judge and compare the data even among member states of the EU. When systems in other countries are then compared, differences in basic system structures complicate interpretation of the variability in implementation even further. Therefore, as stated above, reported case numbers from the EU and worldwide must only be evaluated in the context of the quality of the surveillance program implemented in the individual countries, and trends must be looked at critically.

Outlook: the rest of the world

There remain many countries with an unknown BSE risk, as materials potentially infected with BSE have been distributed throughout the world (Office International des Epizooties, 2001). In a joint WHO/FAO/OIE Technical Consultation on BSE in June 2001, it was therefore concluded that all countries should evaluate their potential exposure through systematic assessment. As well, it is important for other countries to know the real BSE distribution worldwide in order to minimize import risks. Historically, however, few countries have undertaken a national risk assessment before detection of their first BSE case. In the same joint meeting it was concluded that countries should strongly consider, on the basis of these risk assessments, the use of appropriate BSE tests on target populations and on a sufficient number of animals, i.e. the development of targeted surveillance systems.

In North America, both Canada and the USA have undertaken quantitative risk assessments. The assessment of Canada (Morley, Chen & Rheault, 2003), published just before the first case was detected, concluded that the likelihood of BSE in Canada was extremely low to negligible. The Harvard risk assessment of the USA (Cohen et al., 2001) also concluded that the nation was highly resistant to any introduction of BSE and that BSE was extremely unlikely to become established in the USA. However, the many uncertainties over export data from Europe and lack of internal data (such as the effectiveness of enforcement of measures), combined with general problems in data validity as previously described, make it difficult to make reliable quantitative assessments of BSE risk. The quantitative and mathematically sophisticated nature of these assessments can lend an air of accuracy and validity to the conclusions that, in truth, they do not possess (Gravenor & Kao, 2003). Without good data, reliance on quantitative predictions is potentially dangerous and current quantitative risk assessments need to be interpreted carefully. Although in Canada and the USA some surveillance has been in place for several years, experience shows that it is likely not sufficient, either in population tested or in number of animals tested, to estimate the extent of the problem. Therefore, in June 2004, the USA began a one-year program to test the whole cattle risk population for one year (Anonymous, 2004).

In South America, several countries have been assessed in the GBR. Most of these are GBR I, one is GBR II. Argentina made their first risk assessment in 1991, and has already updated it several times. In the countries not assessed in the GBR, no risk assessment has been undertaken, often BSE is not notifiable, and the implementation of surveillance is in the initial stages (van Gelderen, Gimeno & Schudel, 2003).

In Asia, one survey on BSE concluded that the majority of Asian countries did not perform a risk assessment (Ozawa, 2003). According to Eurostat data, however, many Asian countries did receive significant amounts of MBM, implying that the BSE agent could have reached them. This was confirmed when Japan reported its first case in 2001. In Asia there are still countries in which notification of BSE is not mandatory. In other countries it is notifiable, but few have a compensation scheme for BSE suspects. This is reflected in the negligible number of suspects in most of these countries. In Japan, a quantitative risk assessment was published after the first case was detected (Sugiura, Ito, Yokoyama, Kumagai, & Onodera, 2003), and only in Japan has an intensive surveillance program been introduced.

Australia and New Zealand have been assessed in the GBR process and are currently categorized as GBR I. Both countries have implemented some surveillance.

From most other regions of the world, there is no information available regarding risk assessment and surveillance systems in place. As well, in most countries, only minimal measures are in place and may not be effectively enforced. Control of the amplification cycle, primarily through control of cattle feed, can significantly decrease the risk of BSE spreading within countries.

Conclusions

The evidence accumulated to date indicates that the control measures put in place since 1988, and especially since 1996 in the United Kingdom, have brought the epidemic under control, and there is no logical reason why the consistent decline seen over the past decade should not continue. Also in most of the other EU member states and many countries with reported BSE cases, measures including a targeted surveillance system, have been implemented.

However, differences in the structure and implementation of surveillance systems lead to variability in the amount and quality of the data available from almost all countries, including some countries of the EU. The variability complicates the ability to interpret and compare results.

Many countries have neither a risk assessment nor a surveillance system for BSE in place. These countries might be exporters of potential risk material to other countries, even though they have not been identified as countries affected with BSE. Because, minimal information exists regarding the BSE situation in these countries, their trading partners are subsequently limited in their ability to assess their own risks.

These uncertainties emphasize the need for all countries throughout the world to assess their risk. Implementation of a targeted surveillance system can at least provide basic information on the BSE status of these countries. As well, implementation and enforcement of some economically feasible proactive measures can act to control, or at least suppress amplification, of BSE at whatever level it is present.

References

Anonymous (2004). Expanded BSE surveillance in the USA. Veterinary Record, 154(12), 346.

Bird, S. M. (2003). European Union's rapid TSE testing in adult cattle and sheep: implementation and results in 2001 and 2002. Statistical Methods in Medical Research, 12(3), 261-278.

Calavas, D., Ducrot, C., Baron, T., Morignat, E., Vinard, J.-L., Biacabe, A.-G., Madec, J.-Y., Bencsik, A., Debeer, S., & Eliasewicz, M. (2001). Prevalence of BSE in western France by screening cattle at risk: preliminary results of a pilot study. Veterinary Record, 149(2), 55-56.

Cohen, J. T., Duggar, K., Gray, G. M. , Kreindel, S., Abdelrahman, H., HabteMariam, C., Oryang, D., & Tameru, B. (2001). Evaluation of the Potential for Bovine Spongiform Encephalopathy in the United States. (http://www.aphis.usda.gov/lpa/issues/bse/risk_assessment/mainreporttext.pdf)

Doherr, M. G., Heim, D., Fatzer, R., Cohen, C. H., Vandevelde, M., & Zurbriggen, A. (2001). Targeted screening of high-risk cattle populations for BSE to augment mandatory reporting of clinical suspects. Preventive Veterinary Medicine, 51(1-2), 3-16.

Doherr, M. G., Oesch, B., Moser, M., Vandevelde, M., & Heim, D. (1999). Targeted surveillance for bovine spongiform encephalopathy. Veterinary Record, 145, 672.

European Commission (EC). (2002). Report on the monitoring and testing of bovine animals for the presence of Bovine Spongiform Encephalopathy (BSE) in 2001. (http://europa.eu.int/comm/food/food/biosafety/bse/bse45_en.pd).

European Commission (EC). (2003). Report on the monitoring and testing of ruminants for the presence of transmissible spongiform encephalopathy (TSE) in 2002. (http://europa.eu.int/comm/food/food/biosafety/bse/annual_report_2002_en.pdf).

European Commission (EC). (2004). Report on the monitoring and testing of ruminants for the presence of transmissible spongiform encephalopathy (TSE) in the EU in 2003, including the results of the survey of prion protein genotypes in sheep breeds. (http://europa.eu.int/comm/food/food/biosafety/bse/annual_report_tse2003_en.pdf).

Gravenor, M. B., Kao, R. R. (2003). Risk assessments on BSE. Veterinary Record., 152(26), 816.

Heim, D., & Kihm, U. (2003). Risk management of transmissible spongiform encephalopathies in Europe. Revue scientifique et technique, 22(1), 179-199.

Morley, R. S., Chen, S., & Rheault, N. (2003). Assessment of the risk factors related to bovine spongiform encephalopathy. Revue scientifique et technique, 22(1), 157-178.

Office International des Epizooties (OIE). (2001). Conclusions and key recommendations Joint WHO/FAO/OIE. Technical Consultation on BSE: public health, animal health and trade in June 2000. (http://www.oie.int/eng/publicat/rapports/en_BSE%20WHO-FAO-OIE.htm).

Office International des Epizooties (OIE). (2004). Chapter 2.3.13. Bovine spongiform encephalopathy. In: Terrestrial Animal Health Code. (http://www.oie.int/eng/normes/MCode/A_00068.htm).

Office International des Epizooties (OIE) (2004). Appendix 3.8.4.. Surveillance and monitoring systems for bovine spongiform encephalopathy. In: Terrestrial Animal Health Code. (http://www.oie.int/eng/normes/MCode/A_00155.htm).

Office International des Epizooties (OIE). (2004). Number of reported cases of BSE worldwide. (http://www.oie.int/eng/info/en_esbmonde.htm).

Ozawa, Y. (2003). Risk management of transmissible spongiform encephalopathies in Asia. Revue scientifique et technique, 22(1), 237-249.

Scientific Steering Committee. (1999). Report on the evaluation of tests for the diagnosis of Transmissible Spongiform Encephalopathy in bovines. (http://europa.eu.int/comm/food/food/biosafety/bse/bse12_en.pdf).

Scientific Steering Committee. (2000a). Opinion of the Scientific Steering Committee on a method for assessing the Geographical BSE-Risk (GBR) of a country or region. (http://europa.eu.int/comm/food/fs/sc/ssc/out68_en.pdf).

Scientific Steering Committee. (2000b). Final Opinion of the Scientific Steering Committee on the Geographical Risk of Bovine Spongiform Encephalopathy (GBR). (http://europa.eu.int/comm/food/fs/sc/ssc/out113_en.pdf).

Scientific Steering Committee. (2002a) Updated opinion on the Geographical Risk of Bovine Spongiform Encephalopathy (GBR). (http://europa.eu.int/comm/food/fs/sc/ssc/out243_en.pdf).

Scientific Steering Committee. (2002b). Opinion on the geographical BSE-risk (GBR) and its evolution over time in the European Union Member States. (http://europa.eu.int/comm/food/fs/sc/ssc/out249_en.pdf).

Scientific Steering Committee. (2002c). Update of the opinion on the Geographical Risk of Bovine Spongiform Encephalopathy (GBR). (http://europa.eu.int/comm/food/fs/sc/ssc/out291_en.pdf).

Scientific Steering Committee. (2002d). Report on the evaluation of five rapid tests for the diagnosis of Transmissible Spongiform Encephalopathy in bovines (2nd Study). (http://europa.eu.int/comm/food/food/biosafety/bse/bse42_en.pdf).

Sugiura, K., Ito, K., Yokoyama, R., Kumagai, S., & Onodera, T. (2003). A model to assess the risk of the introduction into Japan of the bovine spongiform encephalopathy agent through imported animals, meat and meat-and-bone meal. Revue scientifique et technique; 22(3), 777-794.

van Gelderen, C., Gimeno, E. J., & Schudel, A. A. (2003). Bovine spongiform encephalopathy in South America: a regional preventive approach. Revue scientifique et technique, 22(1), 227-236.

Wells, G. A., Scott, A. C., Johnson, C. T., Gunning, R. F., Hancock, R. D., Jeffrey, M., Dawson, M., & Bradley, R. (1987). A novel progressive spongiform encephalopathy in cattle. Veterinary Record, 121(18), 419-420.

Wilesmith, J. W., Ryan, J. B., & Atkinson, M. J. (1991). Bovine spongiform encephalopathy: epidemiological studies on the origin. Veterinary Record., 128(9), 199-203.

Wilesmith, J. W., Wells, G. A., Cranwell, M. P., & Ryan, J. B. (1988). Bovine spongiform encephalopathy: epidemiological studies. Veterinary Record, 123(25), 638-644.