日本における牛海綿状脳症(BSE)安全対策

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Bovine Spongiform Encephalopathy (BSE) Safety Measures in Japan

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ABSTRACT. Since the first identification of bovine spongiform encephalopathy (BSE) in Japan in September 2001, a series of safety measures was introduced by the Ministry of Agriculture, Forestry and Fisheries, the Ministry of Health, Labour and Welfare and the Food Safety Commission of the Cabinet Office. These measures included blanket BSE testing and removal of specified risk materials at slaughterhouses, surveillance of risk animals and a ban on the use of meat-and-bone meals and traceability on all farms. The Japanese experience over the past five years has shed light on several issues in countries that have a low BSE incidence.
KEY WORDS: bovine spongiform encephalopathy, control, Japan, public health, risk assessment.

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The first case of bovine spongiform encephalopathy (BSE) in Japan was identified in September 2001. In consequence, a series of safety measures were introduced and implemented by three government bodies, as follows:

— the Ministry of Agriculture, Forestry and Fisheries (MAFF), responsible for disease control of cattle on farms
— the Ministry of Health, Labour and Welfare (MHLW), responsible for cattle in slaughterhouses
— the Food Safety Commission of the Cabinet Office, created in July 2003, and its Prion Expert Committee, responsible for the assessment of BSE-related risk.

The measures which were enforced to assess and manage BSE risk by these authorities are summarised in Table 1.

As of May 2006, a total of 9 cases were diagnosed in Japan by active surveillance of cattle on farms and 18 cases through screening tests of all cattle in slaughterhouses.

As in any other country, the occurrence of the first BSE case had a nationwide effect on consumer confidence towards the safety of beef. However, the measures implemented by the government after the diagnosis of the first BSE case, especially after blanket BSE testing of all cattle in slaughterhouses since October 2001, have been successful in restoring confidence. Japanese experience in the control of BSE over the past five years has shed light on several issues in countries that have a low BSE incidence rate.

HISTORICAL SUMMARY OF PRION DISEASES IN JAPAN

In 1976, research on prion diseases in Japan commenced with the establishment of the Slow Virus Research Committee by the MHLW. As the first mouse model of Creutzfeldt-Jakob disease (CJD) was developed at that time [11], the Committee mainly focused on CJD. In the 1980s, scrapie became another focus of interest after the isolation of the scrapie agent from sheep imported from Canada [9]. The results of the work performed by this research group contributed to the scientific basis for subsequent BSE measures, such as the development of immunohistochemistry techniques in mid-1980s [6]. The Committee is still active and now places special emphasis on CJD.

In 1997, in response to the publication of the first cases of variant Creutzfeldt-Jakob (vCJD) disease in the United Kingdom, the MAFF and MHLW formed independent research groups to investigate prion diseases, with members of the above-mentioned research committee as core researchers. The studies of these groups have covered both basic and practical aspects of prion diseases, such as pathogenesis and diagnosis, as well as decontamination. The Western blot technique was improved and a panel of monoclonal antibodies against prion protein was produced as a result of their research [4, 10]. Thus, these two research groups contributed significantly to the implementation of safety measures in Japan when the first BSE case was identified. Both groups are still active.

Passive surveillance of BSE commenced in April 1996. In April 2001, active surveillance of farm cattle showing neurological signs was initiated using rapid commercial BSE test kits. As only a small number of samples (less than 300) had been obtained by the end of April 2001, the criteria for sample collection were expanded and all animals that were recumbent were included in the target population. During surveillance, a five-year-old dairy cow was found to be recumbent at a slaughterhouse and was confirmed as a BSE case on 10 September 2001 [5, 13].

On 27 September 2001, a series of food safety measures, including the removal of specified risk materials (SRM), was introduced. On 4 October, a complete ban on the use of meat-and-bone meal (MBM) was implemented by MAFF.

On 2 October 2001, a training course on the Bio-Rad antemortem BSE test kit (an ELISA test) was held for meat inspectors at 117 meat inspection centres under the supervision of the MHLW. Upon completion of the ELISA training course, the screening programme for BSE was introduced at slaughterhouses for cattle of all ages on 18 October 2001.

Table 1. Risk assessment and management for bovine spongiform encephalopathy in Japan

Date		Ministry of Agriculture, Forestry and Fisheries	Ministry of Health, Labour and Welfare	Food Safety Commission
1996	April	Passive surveillance Administrative guidance on feed ban of MBM for cattle		
1997	April	BSE designated a notifiable disease in the contagious diseases of domestic animals prevention law		
2001	Apr	Active surveillance		
	Oct	Complete ban of importation of MBM Complete feed ban of MBM for all animals Enhanced active surveillance	Removal of SRM (CNS, distal ileum, eye) BSE testing on cattle of all ages in slaughterhouses	
2003	July			Creation of Food Safety Commission
	Dec	Bovine traceability system at production level		
2004	Feb		Vertebral column included in SRM	
	Apr	BSE test for all dead cattle over 24 months mandatory		
	Sept			Comprehensive review of measures on BSE in Japan
	Dec	Bovine traceability system at market distribution level		
2005	Mar	All feed factories have exclusive production lines		
	May			Food safety risk assessment related to BSE measures (change of testing age)
	Aug	Enforcement of notification of imported compound feed	Age of BSE testing changed (cattle over 21 months)	
	Dec			Risk assessment of imported beef from USA and Canada

MBM meat-and-bone meal.
SRM specified risk materials.
CNS central nervous system.
BSE bovine spongiform encephalopathy.

NUMBER OF BSE CASES IN JAPAN

Between October 2001 and the end of March 2006, a total of 5,527,913 cows were screened in slaughterhouses. By 16 May 2006, a total of 18 BSE cases had been confirmed (http://www.mhlw.go.jp/houdou/0110/h1018-6.html). Surveillance of animals at risk first covered limited numbers but reached 100% by April 2004. In 2005, a total of 95,310 head of cattle were tested, and 3 BSE cases were confirmed. By the end of March 2006, surveillance had covered the testing of a total of 247,781 cows. As of May 2006, a total 9 BSE cases were detected through these surveillance measures (http://www.maff.go.jp/soshiki/seisan/bse/bse-i.htm).

These 27 BSE cases found by screening at slaughterhouses and by surveillance on farms were classified into five groups, depending on the year of birth as shown in Table 2. None of these cases showed clinical signs specific of BSE besides symptoms such as dislocation. Two cases (case 8: a 23-month-old steer, case 24: a 169-month-old beef cow) showed Western blot patterns different from those of the other BSE cases, indicating atypical cases [12].

Table 2. Twenty-seven cases of bovine spongiform encephalopathy classified depending on the year of birth

Year of birth	Cases	
	Screening	Surveillance
Before 1995	24	
1995, 1996*	2, 3, 4, 5, 6, 7, 10, 13, 16, 19	1, 11, 15
1999	12, 18	
2000	20, 23	14, 17, 21, 22, 26, 27
2001**, 2002	8, 9, 25	

MBM meat-and-bone meal.
* 1996: notification of MBM ban.
** 2001 complete MBM ban by law.

RISK FACTORS OF BSE IN JAPAN

Outcome of epidemiological investigations into BSE in Japan

In September 2002, MAFF convened a BSE epidemiological study group within the Ministry's BSE Technical Committee to investigate the source of infection and routes of transmission for the seven BSE cases that had been confirmed at that time.

The following risk factors were considered as the principal objective of the investigation: imports of live cattle, imports of MBM and of animal fat used as milk replacer.

Import statistics were analysed for all countries of origin where BSE had been reported at that time. In the report published in September 2003 [7], the countries of origin of potential BSE-infectious materials or live cattle as the

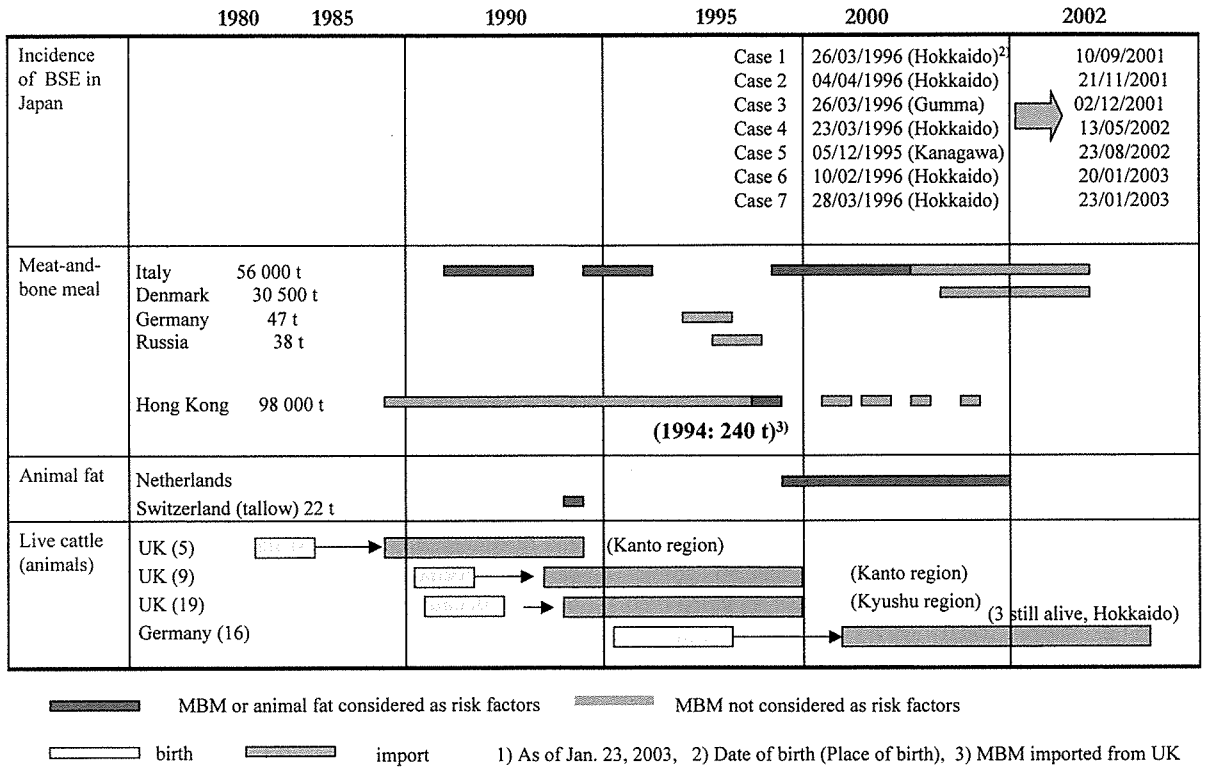

Fig. 1. Investigation into the source of infection of seven BSE cases[1].

potential infection source are listed and shown in Fig. 1.

Source of infection

(1) It is reasonable to assume that the BSE agent originated in the United Kingdom and was imported from there, either directly or indirectly. In this respect, candidates for infection were live cattle (from the Canada, Germany and the United Kingdom), MBM from Italy and animal fat from the Netherlands.

(2) It is possible that live cattle imported from the United Kingdom in 1982 or 1987 included BSE-infected animals. These cattle may have eventually contributed to a load of BSE-infectivity circulating in Japanese cattle feeds, after they had been slaughtered and their slaughter by-products rendered as MBM. Finally these potential sources of infection could have been recycled and amplified in the Japanese cattle population, becoming the source of infection for further cattle at risk.

(3) The live cattle imported from Germany are unlikely to be the source of infection, considering the timing of BSE incidence in Japan.

(4) It is considered highly unlikely that the live cattle imported from Canada were the source. However, relevant data are limited at present and it may be necessary to re-examine this information depending on future findings.

(5) The possibility cannot be ruled out that MBM imported from Italy before 1990 contained the BSE agent, that domestic cattle were exposed to this and were subsequently processed as MBM after slaughter, dismembering and rendering, and that they then became the source of infection.

(6) The animal fat imported from the Netherlands is unlikely to have contained animal protein and is therefore thought unlikely to have been contaminated with the BSE agent. Although we cannot ignore the fact that this animal fat is common to all seven cases in Japan to date, the results of our hypothesis-verification, case-control study and quantitative risk assessment revealed no indication that any of the seven cases could be linked directly to this potential source of infection.

Infection routes

Of the infection sources outlined above, the infection route through MBM is inconceivable through direct feeding, since none of the affected farms fed MBM to their cattle. However, BSE-positive cases were discovered in which feed for cattle, swine and poultry shared the same production lines in compound feed factories. These could have caused cross-contamination of compound feed for cattle during manufacturing or shipping. Considering a large number of cases of animals BAB (born after the ban) in the

United Kingdom, it is thought highly likely that infection in Japan was also caused by cross-contamination.

Animal fat was regularly added as an ingredient in milk replacers and could have been an indirect or secondary source of infection if it had been cross-contaminated with the BSE agent. As stated above, however, there is no proof or indication that any of the seven cases could be linked directly to this potential source of infection.

Scrapie as a potential source of infection in Japan

The number of sheep and goats in Japan is only 10,000 sheep and 21,000 goats.

In Japan, scrapie was first identified in 1984. Since then, a total of 63 cases have been confirmed, all of which were in sheep.

Since May 2001, surveillance for scrapie has been conducted at the level of slaughterhouses; sheep over 24 months of age (and over 12 months since April 2004) using the Western blot method and later the ELISA. By June 2004, approximately 600 sheep had been tested, but no scrapie-positive cases were detected. As the number of sheep is so low, BSE risk analysis has not been conducted.

SURVEILLANCE

Active surveillance was initiated in April 2001 by testing risk animals. In September 2001, surveillance was enhanced and a notification was issued enforcing compulsory testing and incineration of cattle displaying central nervous system symptoms. However, the surveillance of all animals at risk was a lengthy process as it was necessary to set up stock points to maintain fallen stock in refrigeration prior to testing and to separate the rendering facility that receives only carcasses of BSE-positive cattle.

There was an issue that carcasses had been left for a long period in poor storage conditions in some cases. Consequently, the use of the Western blot technique and immunohistochemistry were used on autolysed and/or deteriorated samples in simulated conditions [1, 14].

As the nationwide testing system of animals at risk was completed in April 2004, testing has become mandatory for all cattle that have died over 24 months of age. In accordance with these measures, by the end of March 2006, BSE testing had been conducted on a total of 247,781 animals at risk: 1,095 animals in 2001; 4,315 animals in 2002; 48,411 animals in 2003; 98,650 animals in 2004; and 95,310 animals in 2005. As a result, in addition to the first confirmed case of BSE, BSE testing revealed eight additional cases by May 2006. All of these cows were incinerated. Although the use of MBM in feed has been banned in Japan since October 2001, the delay in the commencement of testing animals at risk made it difficult to grasp the true status of BSE contamination in Japan.

The annual BSE incidence rate per million of animals over 24 months of age was 1.44 in 2001, 0.97 in 2002, 1.96 in 2003 and 2.49 in 2004. In 2004, the positive ratio of BSE through active monitoring was 0.0004%, whereas that with passive surveillance could not be calculated.

CONTROL MEASURES IN CATTLE

Since October 2001, several measures to prevent BSE spread in cattle have been implemented. They include the following:

(1) a complete ban on the use of MBM in feed for all animals
(2) incineration of all SRM
(3) incineration of all carcasses and by-products of confirmed BSE cases and of BSE-positive tested cattle at slaughterhouses
(4) a ban on MBM imports from all countries.

Few tests have been conducted on feed produced in Japan to determine whether MBM had been mixed into the feed (724 tests were conducted between October 2001 and the end of March 2004). MBM has been detected in only one case: in February 2005, protein derived from poultry was detected in cattle feed at a compound feed plant where cattle feed and poultry/pig feed containing chicken meal were produced on the same production line.

Japan relies on imports for approximately 90% of its concentrate feed, such as feed grains, which are used as raw materials in the domestic production of compound and mixed feed. Although imports consist mostly of single-ingredient feed, such as grain, compound feed and mixed feed manufactured overseas are also imported, but to a minor extent (<0.5% of the total amount used in Japan). As the true situation with regard to BSE contamination in exporting countries is unclear, there is no way of predicting whether it is possible to prevent compound or mixed feed that has been adulterated with MBM from being imported into the country. Consequently, the ingredients that are included in compound or mixed feed will be added to the items for which feed importers must submit notification.

A decision was taken in June 2003 to separate compound feed production lines for cattle from MBM production lines in rendering plants. This was implemented fully in April 2005. Carcasses of animals at risk subjected to active surveillance are disposed of in a separate rendering facility and the resulting MBM is incinerated.

The cattle traceability system was initiated in January 2002. In December 2003, traceability was made mandatory in the production stage, and subsequently in the market distribution stage in December 2004. This system enabled identification of each cow born in or after July 2003.

PUBLIC HEALTH MEASURES AT SLAUGHTERHOUSES

Cattle

Since October 2001, blanket BSE testing has been implemented at slaughterhouses at both prefecture and city government levels. The test is performed by meat inspectors who are civil servants and have a veterinarian licence. In

April 2005, testing was changed to cattle over 21 months of age. However, blanket BSE testing will continue for an additional period of three years and will be subsidised by the government for reasons of consumer confidence.

Removal of SRM (head, excluding the tongue and cheek flesh, spinal cord, distal ileum) has been mandatory since October 2001. Removal of the tonsil was added in October 2002 and the removal of the vertebral column containing the dorsal root ganglion in February 2004.

Accumulation of relatively small amounts of abnormal prion protein was found in the peripheral nerves and adrenal glands by the Western blot method in some BSE-positive animals that were subjected to a comprehensive examination. As these tissues are not listed in SRM, a further study on the distribution of BSE prion in these tissues is ongoing [2, 3].

The use of a spinal cord suction apparatus to remove the spinal cord prior to the splitting of carcasses was introduced gradually and is now used in 90% of slaughterhouses.

As of January 2005, there are 6 facilities of a total of 160 slaughterhouses that do not perform carcass splitting. Of the 154 facilities in which carcass splitting is performed, nearly 100% (from 99.4% to 100%) have implemented techniques to prevent the spread of spinal cord tissue on the carcass. Furthermore, there are 125 facilities (91.9%) that conduct suction removal of the spinal cord prior to carcass splitting. The removal by suction of spinal cord tissue is effective in 52.5% to 99.1% of cases, but washing the dressed carcass and removing the spinal cord dura matter after splitting results in the carcass being 100% free of any visible contamination with spinal cord fragments. However, tests detecting a marker protein contained in the spinal cord, glia fibrillary acidic protein (GFAP) have, in some cases, shown minute traces of GFAP on the surface of the lower portion of the carcass. The absence of spinal cord fragments after splitting is confirmed visually by meat inspectors on each animal. All saws, knives and other utensils are washed and disinfected after the slaughter of each animal. Furthermore, the removal of the spinal cord and washing of the carcass greatly reduces the risk of BSE contamination of the meat [8].

The pithing procedure during the slaughtering process is used in approximately 70% of all slaughterhouses in Japan (used on an estimated 80% of all slaughtered cattle). Pithing involves inserting a wire-like instrument into the head of the stunned animal to destroy the spinal nerve tissue, thereby preventing kicking reflexes by the animal. As the MHLW does not yet have sufficient grounds to ban this procedure, the Ministry has not yet announced any measures to ban pithing.

At the beginning, when a series of control measures were implemented, removal of SRM, together with the procedures at slaughter were not sufficient to protect human health. This is shown by the fact that the vertebral column was not included into the SRM list and that the spinal cord was not removed before splitting. We consider that such a risk, associated with incomplete removal of SRM and possible contamination of meat with SRM during slaughter, was overcome by blanket BSE testing as the cattle confirmed BSE-positive were removed from the food chain. As the traceability system was not available at that time, the adoption of blanket BSE testing was also effective in regaining consumer confidence.

Sheep and goats

The removal of the head, excluding the tongue and cheek flesh, spinal cord, tonsil, spleen and intestine of all sheep and goats at slaughterhouses was implemented in April 2002.

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