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Response of Japan to the introduction of exotic animal diseases

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Summary

The response of Japan to the introduction of exotic animal diseases is used as an example of methods used to control these diseases. Japan had been free from the major animal exotic diseases for many years until outbreaks of foot and mouth disease (FMD) occurred in 2000, highly pathogenic avian influenza (HPAI) in 2004 and bovine spongiform encephalopathy (BSE) was detected in 2001. In spring 2000, four outbreaks of FMD were recorded. In early 2004, four outbreaks of HPAI were recorded. Without resorting to vaccination, both diseases were eradicated in several months through depopulation of infected farms, movement controls, surveillance and other measures. The first case of BSE was detected in September 2001. Since then, 23 additional cases were detected by the end of March 2006, despite a strict ban on the use of meat-and-bone meal for feed and other eradication measures. The authors describe how these diseases occurred or were detected in Japan and discuss how Japan responded to them. Details are given on how they were introduced into Japan, the impact on Japanese farming and society and the lessons learned.

Keywords

Animal diseases, Bovine spongiform encephalopathy, Contingency plans, Economic impact, Emergency response, Eradication, Foot and mouth disease, Highly pathogenic avian influenza, Japan.

La reazione del Giappone all'introduzione di malattie animali esotiche

Riassunto

La reazione del Giappone all'introduzione di malattie animali esotiche viene presentata come esempio dei metodi utilizzati per controllare queste malattie. Il Giappone non è stato contaminato dalle maggiori patologie animali esotiche per molti anni fino all'insorgere dell' afta epizootica avvenuta nel 2000, dell'influenza aviaria altamente patogena (HPAI) nel 2004 e dell'encefalopatia spongiforme bovina (BSE) è stata scoperta nel 2001. Nella primavera del 2000 sono stati registrati quattro focolai di afta epizootica. Nei primi mesi del 2004, sono stati registrati quattro focolai di HPAI. Senza ricorrere alla vaccinazione, entrambe le patologie sono state eliminate nell'arco di parecchi mesi attraverso l'abbattimento totale degli allevamenti infetti, i controlli degli spostamenti, la sorveglianza e altre misure. Il primo caso di BSE è stato scoperto nel settembre del 2001. Da allora, sono stati scoperti altri 23 casi alla fine del marzo del 2006, nonostante un bando rigoroso sull'uso della farina di carne ed ossa per il mangime ed altre misure di eradicazione. Gli autori descrivono come si sono verificate queste patologie o come sono state scoperte in Giappone e discutono sulle soluzioni adottate.

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Vengono forniti dei dettagli sulle modalità con le quali sono state introdotte in Giappone, l'impatto sull'agricoltura e sulla società giapponese e sugli insegnamenti appresi.

Parole chiave
Afta epizootica, Encefalopatia spongiforme bovina, Eradicazione, Giappone, Impatto economico, Influenza aviaria altamente patogena, Patologie animali, Programmi di contingenza, Soluzione di emergenza.

Introduction

The geographic advantage of being surrounded by sea and strict import controls on animals and animal products from countries with exotic diseases had protected Japan from the introduction of major exotic diseases for many years until outbreaks of foot and mouth disease (FMD) occurred in 2000, highly pathogenic avian influenza (HPAI) in 2004 and the first case of bovine spongiform encephalopathy (BSE) was detected in 2001. The response mechanisms described in this paper are examples of methods used in Japan to respond to the introduction of exotic diseases.

Import control of animals and animal products

Import control policy and animal health requirements that apply to animals and animal products from foreign countries are implemented by the Animal Health Division of the Ministry of Agriculture Forestry and Fisheries (MAFF) in accordance with the Office International des Épizooties (OIE: World organisation for animal health) *Terrestrial animal health code* (13) and Domestic Animal Infectious Diseases Control Law (1). In close collaboration with the Animal Health Division, the Animal Quarantine Service conducts import quarantine of animals and import inspection of animal products at 51 ports and 36 airports nation-wide. It is through these ports that animals and animal products are permitted entry into Japan. Import prohibition applies to animals and animal products from countries with FMD, rinderpest or African swine fever, which are designated as malignant exotic animal diseases under the Domestic Animal Infectious Diseases Control Law.

Eradication and control of exotic diseases

Eradication measures against exotic diseases are taken in accordance with the Domestic Animal Infectious Diseases Control Law. This law prescribes notification of suspected animals, isolation and depopulation of infected premises, establishment of movement control areas, payment of compensation and other measures that should be taken in the event of the introduction of an exotic disease.
Eradication measures are implemented by prefecture veterinary inspectors (veterinarians), who are appointed by prefecture governors, with the support of voluntary defence organizations and private veterinarians, under the guidance and instructions of the MAFF. There are 175 prefecture Livestock Hygiene Service Centres (LHSC) located across Japan, which are responsible for taking samples or making a preliminary diagnosis of an exotic disease. Confirmatory diagnosis of exotic diseases is made by the National Institute of Animal Health (NIAH).

Bovine spongiform encephalopathy control measures

Measures for BSE control are taken not only in accordance with the Domestic Animal Infectious

Diseases Control Law (Law No. 166, 1951), but also the Law Concerning Assurance of the Safety of Feed and Improvement of Quality of Feed (Feed Safety Law) (Law No. 35, 1953) and the Law on Special Measures against BSE (Law No. 7, 2002). The Feed Safety Law was amended in October 2001 so that it prescribes the prohibition of the use of processed animal protein for animal feed. The Law on Special Measures against BSE was enforced in July 2002 and prescribes the following:

- prohibition of the importation and use of meat-and-bone meal (MBM) of bovine origin for feed
- performing BSE tests on all cattle over a designated age that are slaughtered for human consumption
- reporting of all dead animals and testing them for BSE
- identification of all cattle born in or imported into Japan.

Inspection of feed mills and sampling and testing of feed components used in animal protein are conducted by National Feed and Fertilizer Stations.

Animal disease contingency plans

When FMD broke out in 2000, the MAFF had a single contingency plan for exotic diseases, namely, the Malignant Exotic Animal Disease Control Guidelines (3). Since then the MAFF has developed contingency plans for specific diseases, in particular: FMD, BSE and HPAI (8, 9, 10). Contingency plans describe specific eradication measures to be taken, in addition to the establishment of emergency management units at various levels, including municipal, prefecture and national government. Details of the outbreaks and the measures taken have been described by Sugiura *et al.* (14).

Foot and mouth disease outbreak in 2000

An outbreak of FMD occurred in Japan in the spring of 2000, the first in 92 years. Between 25 March and 11 May, four farms were infected. The disease was eradicated, without resorting to vaccination, through a campaign of culling, movement controls of cloven-hoofed animals in areas surrounding infected premises and intensive clinical and serological surveillance.

How the disease broke out

On 8 March 2000, a beef farmer in the Miyazaki prefecture found one of his cattle showing pyrexia, anorexia and coughing. A private veterinarian visited the farm on 12 March and observed clinical signs of anorexia and nasal and mouth erosions in other cattle. The veterinarian reported the observations to Miyazaki LHSC on 21 March. Diagnostic samples were taken and sent to the Department of Exotic Diseases of the NIAH on 22 March. On that day, a sample of epithelium sent to the NIAH was examined for the presence of FMD antigen using the antigen capture enzyme–linked immunosorbent assay (ELISA) and the complement fixation test; both tests were negative. On 23 March, a gene segment of FMD virus type O was detected by reverse transcriptase–polymerase chain reaction (RT-PCR) in epithelium tissue from an animal with clinical signs. The international standard procedures, as described in the OIE *Manual of diagnostic tests and vaccines for terrestrial animals*, were used to perform these tests (12). On 24 March, serum samples from nine animals had high antibody titres against FMD in the liquid–phase blocking (LPB) ELISA; on 25 March, all ten animals on the farm were assessed as being infected with FMD. On the basis of the estimated exposure date, this farm was later considered to be the index case. The sequence data of the detected gene segment was sent to the

OIE international reference laboratory for FMD, the Institute for Animal Health in Pirbright, for comparison with other FMD isolates.

Following this outbreak, the disease spread locally to two other farms in the Miyazaki prefecture by early April. In May, one feed-lot farm in the Hokkaido prefecture was confirmed as being infected by FMD. Details of these infected farms are presented in Table I. Figure 1 shows the location of these outbreaks.

How Japan responded

Eradication measures were based on the following:

- immediate depopulation of infected farms
- movement controls of cloven-hoofed animals in the areas surrounding the infected farms
- intensive epidemiological surveillance of farms in contact with the infected farms
- nationwide clinical and serological surveillance and diagnostic investigation of any animals showing clinical signs suggestive of FMD.

Task forces were established at national, prefecture and municipal levels to implement these eradication measures.

Depopulation of infected farms

Immediately after diagnosis of FMD was confirmed, all animals on the four infected farms were destroyed. Feed, bedding materials, manure and compost were buried. Housing facilities and equipment used for handling the animals were disinfected. Stamping-out on the first three infected farms was completed in a single day, while four days were required to complete stamping-out on the fourth infected farm. A total of 740 animals were destroyed.

Movement controls

On 25 March, when the first outbreak was suspected, a movement control area, with a 20 km radius, was established. On the same day, a surveillance area, with a radius of between 20 and 50 km, was also established around the primary outbreak.

The movement of cloven-hoofed animals, farm equipment and other goods, that had the potential of becoming mechanical vectors of infection, was prohibited. Livestock markets and slaughterhouses were closed and artificial insemination practices were prohibited in this area.

On 23 April, the restrictions in the surveillance area were lifted and the movement control area was reduced to a radius of 10 km around the second and third infected farms. On 26 April, the movement control area was further reduced to an area with a radius of 10 km around the third infected farm; this restriction was lifted on 2 May. On 11 May, when the fourth outbreak was confirmed in Hokkaido, a movement control area of 10 km in radius was established around this outbreak; this was lifted on 9 June.

Roadblocks and disinfection points were established on main roads bordering the movement control and surveillance areas. Vehicles transporting feedstuffs and milk were disinfected at these points.

Clinical surveillance

Between 25 March and 9 June, a total of 93 225 farm visits were made by prefecture veterinary inspectors for clinical surveillance purposes. In the same period, 143 306 farm visits were made by private veterinarians. All farms in the movement control and surveillance areas, and some other farms in other parts of the country, were included in this clinical surveillance programme. As a result, 31 suspect cases were reported to the MAFF and diagnostic samples were submitted to the NIAH. No additional case of FMD was diagnosed; the tests performed were the LPB-ELISA, sandwich ELISA (S-ELISA) on serum samples, the RT-PCR and virus isolation in cell culture on swabs of the lesions and probang samples. All test results were negative.

Serological surveillance

After the first outbreak, serum samples were collected from all cattle on farms in the movement control and surveillance areas, from cattle on farms that had introduced animals in the preceding three

Table I
Location, number of susceptible animals, clinical signs and results of laboratory investigations of foot and mouth disease outbreaks in Japan in 2000

Outbreak and location	Number of susceptible animals	Date of diagnosis	Date of completion of stamping-out	Number of animals destroyed	Movement control area applied	Clinical signs	Laboratory verification
1. Miyazaki city Miyazaki prefecture	10 fattening cattle	25 March	26 March	10	25 March-22 April	Nasal and mouth erosions	Type O (liquid-phase blocking ELISA, RT–PCR)
2. Takaoka town Miyazaki prefecture	6 breeding cows and 3 calves	3 April	4 April	9	3 April-25 April	No clinical signs	Type O (liquid–phase blocking ELISA)
3. Takaoka town Miyazaki prefecture	10 breeding cows and 6 calves	9 April	10 April	16	9 April-2 May	Salivation and anorexia	Type O (liquid–phase blocking ELISA,virus isolation)
4. Honbetsu town Hokkaido prefecture	705 fattening cattle	11 May	15 May	705	11 May-9 June	No clinical signs	Type O (liquid–phase blocking ELISA, RT–PCR)

ELISA enzyme-linked immunosorbent assay
RT-PCR reverse transcriptase-polymerase chain reaction

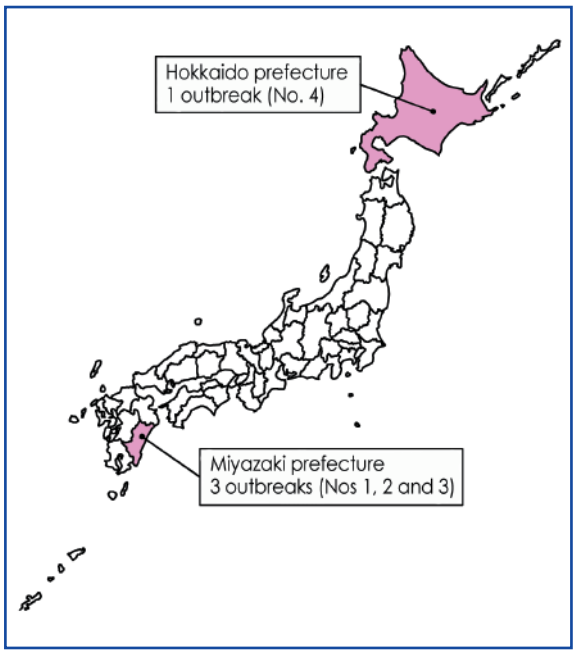

Figure I
Location of foot and mouth disease outbreaks in Japan in 2000
(Numbers in brackets correspond to those given in Table I)

months from farms in the quarantine areas and from farms that had imported forage for animal feed. The second and third infected farms were detected as a result of this serological surveillance and 60 farms were suspected of harbouring infection. Of these 60 farms, one farm in Hokkaido (the fourth infected farm) was classed as infected, based on the presence of sero-positive animals, a rise in antibody titres in some animals and a positive RT-PCR on probang material; two positive animals were identified on this farm.

How the disease was introduced into Japan

The sequence data of the VP1 gene of the FMD virus from an animal on the primary outbreak farm indicated that the virus was a close match to the type O viruses isolated in countries in East Asia. This and other facts supported the hypothesis that wheat straw, which originated from the People's Republic of China, carried the FMD virus to Japan (4). Other possible sources were considered,

but no evidence was found to suggest any other means of introduction of FMD into Japan.

Impact of FMD introduction on farming and society

Direct economic costs arising from the FMD outbreak in 2000 consisted of compensation to farmers of infected premises, cost for destruction and burial of infected animals, laboratory testing for serological surveillance and confirmatory diagnosis, and voluntary control measures (disinfectants, awareness programmes, etc.). These cost 882 million yen (approximately US$7.6 million) (5). In addition to these costs, the MAFF imported one million doses of FMD vaccine for emergency use.

Beef consumption declined temporarily after the first outbreak, but recovered to normal levels after a short period of time. This was because consumers were informed at an early stage that FMD is not zoonotic: the MAFF issued a press announcement every day describing the disease situation, informing the public that the disease was not zoonotic and that FMD is not contracted by consuming beef or milk produced from infected animals. In spite of the small decline in beef consumption, a budget totalling 6 billion yen (approximately US$51.8 million) was allocated to promote consumption of animal products, to cover other losses that farmers had suffered and to stabilise beef prices for calves and heifers. Indirect economic losses arising from import suspensions by other countries were minimal because Japan exports only a small amount of beef.

As wheat straw imported from China was considered to be the source of infection, importation of wheat and rice straw and other forage from China and other FMD-infected countries was banned in May 2000, unless it has been heat-treated. To alleviate the shortage of forage, due to the prohibition of imports, 1 800 million yen (approximately US$16 million) was allocated to promote domestic straw production.

Highly pathogenic avian influenza outbreak in 2004

An outbreak of HPAI was diagnosed in Japan in early 2004, the first for 79 years. Between 12 January and 1 March 2004, four farms were infected. The disease was eradicated, without resorting to vaccination, through a campaign of culling, movement controls on poultry and intensive surveillance.

How the disease broke out

A poultry layer farmer in the Yamaguchi prefecture found dead chickens on his farm on 28 December 2003 and reported his observation to a LHSC on 30 December. An inspector of the LHSC visited the farm and took samples for virus isolation on 9 January 2004. A virus with haemagglutination activity was isolated and sent to the NIAH on 11 January for subtype identification. The virus was confirmed as subtype H5 the following day. The virus was identified to be an N1 subtype using the conventional neuraminidase inhibition (NI) assay. The virus was found to be highly pathogenic using the OIE standard procedure (12).

The second outbreak of HPAI was detected in a backyard flock in the Oita prefecture on 17 February. A farmer, who had found three of his bantams dead, reported his observation to a LHSC on 14 February. An inspector of the LHSC visited the farm and took samples for virus isolation the same day. On 17 February, samples were also sent to the NIAH, where an avian influenza virus subtype H5N1 was isolated.

The third outbreak was detected on a layer farm in the Kyoto prefecture on 29 February. The farmer observed high mortality in chickens on 17 February and reported the mortality to a LHSC on 27 February. An inspector of the LHSC visited the farm that day and took samples, which were sent to the NIAH. The NIAH isolated an avian influenza virus subtype H5 on 29 February.

The fourth outbreak was detected on a broiler farm 4 km north-east of the third outbreak. Increased mortality was observed on 3 March. Samples were sent to the NIAH on 5 March. An AI virus subtype H5N1 was detected on 8 March. Details of these outbreaks (infected farms) are given in Table II and Figure 2.

How Japan responded

Eradication measures were based on the following principles:

- immediate depopulation of infected farms
- movement controls on chickens and other poultry within a radius of 30 km around the infected farms
- intensive surveillance of farms in the movement control areas and farms epidemiologically related to the infected farms.

Task forces were established at national, prefecture and municipal levels to implement these measures.

Depopulation of infected farms

Immediately after diagnosis of HPAI, all chickens

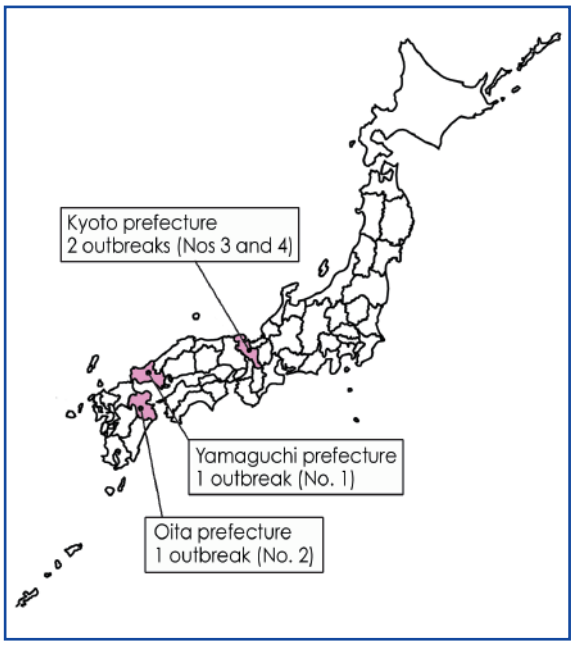

Figure 2
Location of highly pathogenic avian influenza outbreaks in Japan in 2004
(Numbers in brackets correspond to those given in Table II)

Table II
Location, number of poultry, clinical signs and results of laboratory investigations of highly pathogenic avian influenza outbreaks in Japan in 2004

Outbreak and location	Number of susceptible birds	Number of birds affected	Date of diagnosis	Stamping-out completed	Number of birds destroyed	Movement control area applied	Clinical signs	Laboratory verification
1. Ato town Yamaguchi prefecture	34 640 layer chickens	28 660	12 January	21 January	34 640	12 January-18 February	High mortality	Subtype H5N1 (virus isolation)
2. Kokonoe town Oita prefecture	13 bantams and 1 duck	14	17 February	18 February	14	17 February-10 March	High mortality	Subtype H5N1 (virus isolation)
3. Tamba town Kyoto prefecture	225 000 layer chickens	123 003	29 February	22 March	225 000	22 March-12 April	High mortality	Subtype H5N1 (virus isolation)
4. Tamba town Kyoto prefecture	15 000 broiler chickens	14 699	3 March	11 March	15 000	22 March-12 April	High mortality	Subtype H5N1 (virus isolation)

NOTE
In addition to the above tour outbreaks, 6 880 chickens, which were shipped from the third outbreak, were destroyed at a poultry processing plant in the Hyogo prefecture

kept on the four infected farms were destroyed. Depopulation was followed by cleaning and disinfection of the chicken houses. Depopulation and disinfection of the four infected farms were completed by 21 January, 18 February, 22 March and 11 March, respectively. A total of 274 654 chickens were destroyed.

Movement controls

On 9 January 2004, when the first outbreak was suspected, the infected farm was quarantined. On 12 January, a movement control area, with a radius of 30 km, was established around the infected farm. In this area, the movement of poultry and all goods that had the potential to spread the disease was prohibited. The movement control was lifted on 18 February, when 21 days had elapsed after the completion of cleaning and disinfection and by which time the Yamaguchi prefecture government had completed all clinical and serological surveillance activities on all chicken farms in the movement control area, with negative results. Likewise, a movement control area, with a radius of 30 km, was established around the second outbreak on 17 February; it was reduced to a radius of 5 km on 28 February and restrictions were lifted on 10 March. A movement control area, with a radius of 30 km, was established around the third outbreak on 29 February, reduced to a radius of 5 km on 1 April and lifted on 12 April. The fourth outbreak was geographically close to the third outbreak so there was no need to re-establish the movement control area for the fourth outbreak.

Surveillance

All chicken farms in the movement control areas were visited by prefecture veterinary inspectors for clinical surveillance. All or some of the commercial chicken farms and hobby chicken farms in the movement control areas were subjected to sampling for serological examination and virus isolation; neither avian influenza antibody, nor virus were detected. In addition, faecal samples from wild birds and water samples from ponds and lakes in the movement control areas were subjected to virus isolation attempts; no AI virus was isolated.

How the virus was introduced into Japan

An epidemiological study team formed by the MAFF concluded that the AI virus was probably introduced into Japan by migratory birds from East Asia (7). The fact that there was a slight difference in the genetic sequence between the viruses isolated in the Yamaguchi, Oita and Kyoto prefectures suggested that the viruses were introduced into these prefectures on separate occasions from East Asia.

Impact of HPAI on farming and society

Compensation to farmers for the depopulation of chickens on the four infected farms totalled 380 million yen (approximately US$3.3 million); this included cleaning and disinfection costs. In addition, 830 million yen (approximately US$7.2 million) was paid to the farmers located in the movement control areas to compensate them for their losses. In addition, 3.2 million doses of AI vaccine were imported for emergency use. Consumption of poultry and eggs declined, which may have been due to the report that products from infected farms in Kyoto had been marketed. However, consumption returned to normal after a short period of time.

Detection of bovine spongiform encephalopathy cases since 2001

The first case of BSE was detected in Japan in September 2001. By 31 March 2006, 23 additional cases had been detected as a result of active surveillance introduced in October 2001.

How the first case was detected

After BSE was designated a notifiable disease in April 1996, brain tissue from between 20 and 36 clinical suspect cases were submitted annually for

histopathological examination until the 2000 fiscal year. In April 2001, surveillance was enhanced by increasing the number of brain samples to be tested, to meet the international standards set by the OIE. On 6 August 2001, a recumbent cow was transported for slaughter to an abattoir in the Chiba prefecture. A brain sample from the cow was sent to a LHSC and, as a result of histopathological examination, vacuoles were found. The brain sample was sent to the NIAH for Western blot and immunohistochemistry. Results of both tests were positive on 10 September 2001. The international standard procedures were used for this testing (12) and diagnosis was confirmed by the OIE international reference laboratory for BSE, the Veterinary Laboratories Agency in Weybridge. The carcass of the first case was condemned on the day of slaughter as being unsuitable for human consumption; it was sent to a rendering plant and processed for MBM. When the cow was later found to be a positive BSE case, the MBM produced from this cow was traced and destroyed.

How Japan responded

The Japanese government has taken various measures to protect the cattle population from exposure to contaminated feed. The importation of live cattle and MBM has been prohibited from the United Kingdom and other BSE-affected countries (except for MBM heat-treated at 133°C, 3 bar for 20 min) since July 1990; the importation of MBM from the United Kingdom has been prohibited since March 1996; an administrative guideline was issued to prohibit the use of ruminant MBM for ruminant feed after April 1996; and the importation of MBM was prohibited from European Union member states, Switzerland and Liechtenstein after January 2001.

After the detection of the first case, the MAFF and Ministry of Health, Labour and Welfare (MHLW) introduced the following public health and animal health measures:

- the mandatory removal and incineration of specified risk materials (SRM) from all cattle slaughtered for human consumption from 27 September 2001; SRM were initially defined as the head (except the tongue and cheek meat), the spinal cord and the distal ileum and extended later to include the vertebral column
- a legal ban on the domestic use of ruminant protein for ruminant feed was implemented on 18 September 2001, followed by a ban on the domestic use and importation of all processed animal proteins for the production of feed for ruminants, pigs and chickens and for fertilizer, effective on 4 October 2001
- destruction of offspring that were born to an infected cow within two years prior to the detection that the dam was BSE-positive and the destruction of cohort animals that had consumed the same feed as the positive animal during the first year of life.

As a result of these measures, no BSE case has been detected in animals born after February 2002.

Surveillance

Immediately after the detection of the first case, BSE surveillance was enhanced, and included mandatory reporting and investigation of all clinical BSE suspects (passive surveillance), testing of fallen stock and all cattle slaughtered for human consumption (active surveillance). The surveillance programme equalled or exceeded that outlined in the *Code* (13).

The BSE surveillance programme detected an additional 23 cases by 31 March 2006. Of the 24 cases, 21 were dairy cows and two were young Holstein steers (21 and 23 months, respectively). The Western blot result was positive, but neither spongiform changes nor PrP deposition were found after pathological and immunohistochemical examination (15). The brain samples from these two young cases were bioassayed into bovinised transgenic mice shortly after the detection of these cases. At 1 November 2006, this transmission study was still underway.

A summary of the BSE cases recorded in Japan is given in Table III and Figure 3.

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Table III
Date of diagnosis, date of birth, place of birth, clinical signs and results of laboratory tests of bovine spongiform encephalopathy cases detected in Japan between September 2001 and March 2006

No.	Date of diagnosis	Date of birth (age)	Type of cattle	Location of farm (prefecture of birth)	Clinical signs	Types of surveillance[a]	Laboratory diagnosis
1	10 September 2001	26 March 1996 (65 months)	Dairy cow	Chiba prefecture (Hokkaido prefecture)	Anastasia	Clinical-suspect	WB, IHC, HP
2	21 November 2001	4 April 1996 (67 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	No clinical signs	Slaughterhouse	WB, IHC
3	2 December 2001	26 March 1996 (68 months)	Dairy cow	Gunma prefecture (Gunma prefecture)	No clinical signs	Slaughterhouse	WB, IHC, HP
4	13 May 2002	23 March 1996 (63 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	Muscular split of left forelimb	Slaughterhouse	WB, IHC, HP
5	23 August 2002	5 December 1995 (80 months)	Dairy cow	Kanagawa prefecture (Kanagawa prefecture)	Hip joint dislocation	Slaughterhouse	WB, IHC
6	20 January 2003	10 February 1996 (83 months)	Dairy cow	Wakayama prefecture (Hokkaido prefecture)	Dystasia	Slaughterhouse	WB, IHC, HP
7	23 January 2003	28 March 1996 (81 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	No clinical signs	Slaughterhouse	WB, IHC
8	6 October 2003	13 October 2001 (23 months)	Holstein steer	Fukushima prefecture (Tochigi prefecture)	No clinical signs	Slaughterhouse	WB[b] (atypical)
9	4 November 2003	13 January 2002 (21 months)	Holstein steer	Hiroshima prefecture (Hyogo prefecture)	No clinical signs	Slaughterhouse	WB[b]
10	22 February 2004	17 March 1996 (95 months)	Dairy cow	Kanagawa prefecture (Kanagawa prefecture)	Dystasia, hip joint dislocation	Slaughterhouse	WB, IHC, HP
11	9 March 2004	8 April 1996 (94 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	Anastasia, hip joint dislocation	Fallen stock	WB, IHC, HP
12	13 September 2004	3 July 1999 (62 months)	Dairy cow	Kumamoto prefecture (Kumamoto prefecture)	No clinical signs	Slaughterhouse	WB, IHC, HP
13	23 September 2004	18 February 1996 (103 months)	Dairy cow	Nara prefecture (Hokkaido prefecture)	Anastasia, hip joint dislocation	Slaughterhouse	WB, IHC, HP

Table III (contd)

No.	Date of diagnosis	Date of birth (age)	Type of cattle	Location of farm (prefecture of birth)	Clinical signs	Types of surveillance[a]	Laboratory diagnosis
14	14 October 2004	8 October 2000 (48 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	Suffocated to death	Fallen stock	WB, IHC, HP
15	26 February 2005	5 August 1996 (102 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	Arthritis	Fallen stock	WB, IHC, HP
16	27 March 2005	23 March 1996 (108 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	No clinical signs	Slaughterhouse	WB, IHC, HP
17	8 April 2005	11 September 2000 (54 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	Anastasia	Fallen stock	WB, IHC, HP
18	12 May 2005	31 August 1999 (68 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	Anastasia, hip joint dislocation	Slaughterhouse	WB, IHC, HP
19	2 June 2005	16 April 1996 (109 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	No clinical signs	Slaughterhouse	WB, IHC
20	6 June 2005	12 August 2000 (57 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	No clinical signs	Slaughterhouse	WB, IHC
21	10 December 2005	13 February 2000 (69 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	Heart failure	Fallen stock	WB, IHC
22	23 January 2006	1 September 2000 (64 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	Abomasum displacement	Fallen stock	WB, IHC
23	15 March 2006	8 July 2000 (68 months)	Dairy cow	Hokkaido prefecture (Hokkaido prefecture)	No clinical signs	Slaughterhouse	WB, IHC, HP
24	17 March 2006	10 February 1992 (169 months)	Beef cow	Nagasaki prefecture (Nagasaki prefecture)	Anastasia	Slaughterhouse	WB, IHC, HP (atypical)

a) clinical-suspect: passive surveillance targeting animals on farms with clinical signs compatible of BSE; Fallen-stock: active surveillance targeting all fallen-stock animals of 24 months of age or older dead on farms or during transportation; Slaughter-house: active surveillance targeting all animals slaughtered for human consumption

b) Diagnosis was made only by Western blot; the brain sample was bioassayed into bovinised transgenic mice shortly after the diagnosis. At 1 November 2006, no further evidence of BSE infection had been observed in the mice

WB Western blot

IHC immunohistochemistry

HP histopathology

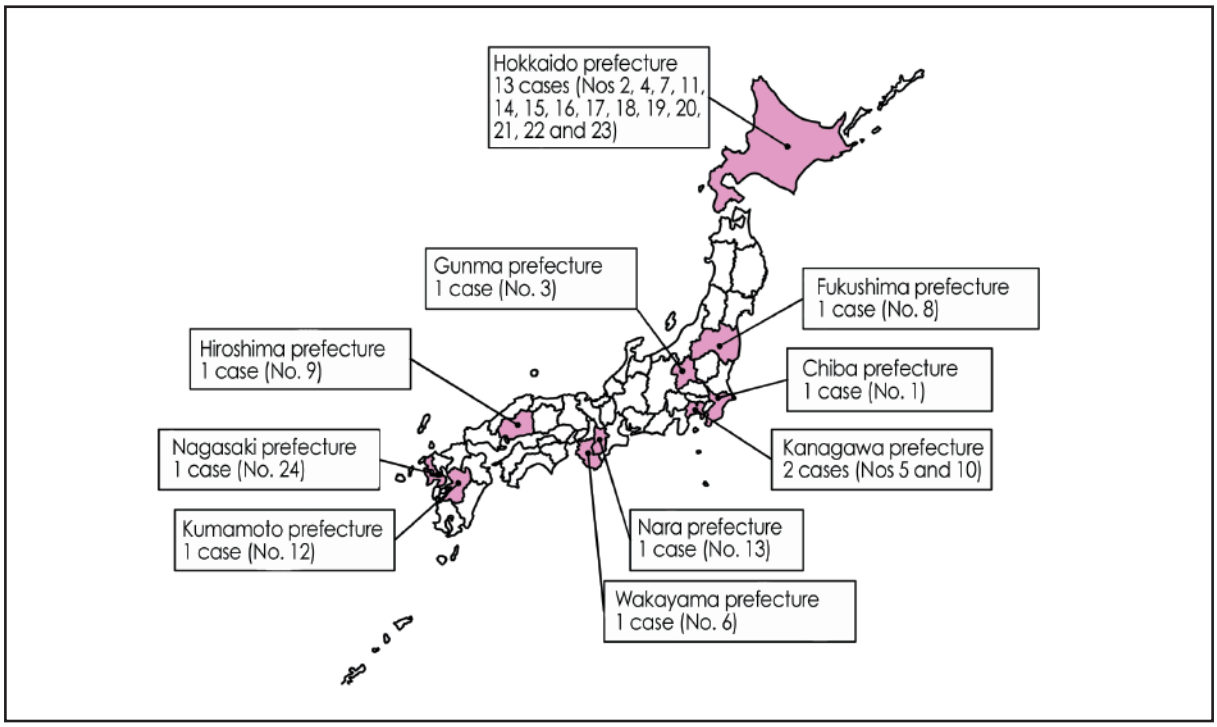

Figure 3
Location of bovine spongiform encephalopathy outbreaks in Japan from September 2001 to March 2006
(Numbers in brackets correspond to those given in Table I)

How the disease was introduced into Japan

Considering the fact that the most of the cases were born between December 1995 and 1996, and susceptibility in cattle peaks in the first year of age, an epidemiological study team formed by the MAFF concluded, in an interim report published in 2003, that the following were possible sources of infection (6):

- contamination with MBM, possibly by feed contaminated with MBM in feed mills in Italy and imported in November 1996; the feed had not been heat-treated at 133°C for 20 min at 3 bars of pressure
- use of contaminated animal fat (powdered animal fat imported from the Netherlands between 1995 and May 1996) in feed for cattle and in milk replacers for calves.

In addition to the above, there was the possibility that the BSE agent might have entered Japan through cattle imported from the United Kingdom in the 1980s, from Germany in 1993, or from MBM imported from countries in Europe before 1995. The possibility that the source of infection may have been MBM from Japan could not be completely excluded. More information on this subject needs to be collected in the future in order to draw more definite conclusions.

Impact of the detection of BSE cases on farming and society

The economic and social repercussions following

detection of the BSE case were enormous. Direct costs included the costs of destruction of the infected animal and cohort animals, enhanced surveillance and public health measures introduced (SRM removal and BSE testing of all cattle slaughtered for human consumption).

Strict feed bans prohibiting the use for feed of processed animal proteins (except pig or poultry proteins produced in a production line that was completely separate from that used for ruminant proteins) were introduced in October 2001. Financial support was provided to renderers for incineration of MBM and for separating production lines in rendering plants.

As beef consumption declined drastically (by 60% after the detection of the first case), measures were taken to stabilise the beef price and to compensate farmers who had suffered economic loss from lower beef prices.

A total budget of 155.4 billion yen (approximately US$1.3 billion) was allocated for these measures in fiscal year 2001 alone. Most of these measures remained in place in subsequent years as well. Beef consumption recovered to 90% of the previous level once testing of all cattle slaughtered for human consumption was introduced.

In an attempt to regain consumer confidence, a traceability system was introduced in 2003, with an identification number inscribed on the ear tag attached to all cattle and detailed labels provided on beef packages; this system enables tracing to the farm of origin.

An investigation committee was established in 2001 to evaluate if the government handled the BSE issue properly (11). The committee concluded that there had not been enough transparency and involvement of scientists during decision-making by the MAFF and MHLW; it recommended that an independent risk assessment agency be established. Based on the recommendations of this committee, the Food Safety Commission, a risk assessment agency independent from the MAFF and MHLW, was established in July 2003.

Lessons learned

The outbreaks of FMD in 2000 and HPAI in 2004 were successfully eradicated in a relatively short time. Early detection of the disease and early reaction to the disease outbreaks were the key to the successful eradication of these diseases. In addition, sharing of available information and risk communications contributed to the successful eradication by securing the cooperation of farmers and minimising over-reaction by consumers.

In contrast, the detection of BSE has had an enormous and long-lasting impact on farming and society due to it being a zoonosis with a long incubation period. Some of the lessons learned from the experience of the outbreaks of FMD, HPAI and BSE are given below.

Early detection: the key to successful eradication of highly contagious diseases

Cattle and pig farmers in the Miyazaki and other southern Kyushu prefectures were placed on alert against the possible introduction of FMD after the FMD outbreak in 1997 and the subsequent FMD infection reported in Taiwan.

After an outbreak of HPAI was reported in the Republic of Korea in December 2003, the MAFF issued a warning on 24 December to prefecture governments that programmes should be established to increase the awareness of farmers and veterinarians in regard to clinical signs of HPAI. This contributed to the early detection of the first outbreak of HPAI in January 2004.

These actions suggest that whenever exotic diseases prevail in neighbouring countries and the risk of introduction of these diseases increases, it is

important that both farmers and veterinarians are warned, so that they can be on the alert for any possible introduction of these diseases. For diseases such as BSE, that have a long incubation period, the assessment of the risk of introduction is more complicated.

Exotic disease contingency plans enable prompt responses

Early reaction to the outbreaks by national and prefecture governments, in cooperation with farmers and veterinarians, also contributed to the early eradication of FMD and HPAI. The MAFF Animal Health Division develops emergency animal disease contingency plans to enable early reaction to outbreaks of exotic diseases. The plans include the establishment of a task force, response measures to be taken and the experts to be consulted in the event of the introduction of an exotic disease. When FMD was introduced into Japan in 2000, the MAFF had only one generic contingency plan for malignant exotic diseases. The Miyazaki prefecture government, after the FMD epidemic in Taiwan in 1997, had developed a contingency plan for possible introduction of FMD into the prefecture. MAFF and prefecture governments reacted according to these plans.

Information provision should not be neglected

During the course of an outbreak, members of a task force become preoccupied with implementation of eradication measures and providing information tends to be neglected. However, establishing an information programme that provides regular updates on the disease situation is important. This helps to keep the public informed and avoids unwarranted speculation brought about by insufficient information. During the course of the FMD outbreak, a press release was published every day, updating the situation on the spread of the disease, the results of surveillance and the number of animals depopulated.

Information provision is particularly important in the event of the introduction of a disease of a zoonotic nature. When the HPAI virus was identified in 2004 and chicken and egg consumption declined, the Food Safety Commission, an independent scientific agency, issued a fact sheet stating that HPAI was not a foodborne disease (2). This contributed to the return to normal of chicken and egg consumption. When the government is forced to introduce a measure that is not scientifically sound to regain consumer confidence, it should explain the scientific value (risk mitigation effect) of the measure being introduced, so that the government will not be put into a difficult situation when it wants to correct these measures at a later date.

Never assume that a country is protected from exotic diseases

As Japan is surrounded by sea and has taken stringent import controls for animals and animal products from countries with exotic disease, it was always thought that the chances of introducing an exotic disease were very slight. However, diseases can be introduced by migratory birds, the international movement of which cannot be controlled, and through feed (forage contaminated with FMD virus, grain feed mixed with MBM that has been contaminated with the BSE agent, etc.), which is not usually subject to import controls. The risk of introduction of exotic diseases should be regularly assessed to identify which exotic diseases pose the greatest risk of introduction. This leads to early detection of disease and facilitates the implementation of the necessary public health measures for zoonotic diseases that have long incubation periods.

References

1. Anon. 2005. Domestic Animal Infectious Diseases Control Law (Law No. 166, 1951). In Official Gazettes of 31 May 1951, 31 March 1952, 1 August 1953, 15 August 1953, 27 August 1955, 24 March 1956, 6 June 1956, 15 September 1962, 5 June 1971, 31 December 1971, 7 May 1975, 5 July 1978, 18 May 1985, 19 December 1989, 11 April 1997, 16 July 1999, 22 December 1999, 22 November 2000, 14 June 2002, 31 July 2002, 13 December 2002, 11 June 2003, 2 June 2004 and 21 October 2005 [in Japanese]. Ministry of Finance Printing Bureau, Tokyo.
2. Food Safety Commission (FSC) 2004. FSC thinks that chicken meat and eggs are safe, 11 March. FSC, Tokyo 2 pp (www.fsc.go.jp/iinkai/i-dai124/dai124kai-siryou5-1.pdf accessed on 1 November 2006).
3. Ministry of Agriculture, Forestry and Fisheries (MAFF) 1976. Malignant exotic animal disease control guidelines (MAFF Livestock Industry Bureau Director General Administrative Notification No. 50-Chiku-A-3843 1975 amended by No. 51-Chiku-A-2760) [in Japanese]. MAFF, Tokyo, 31 pp.
4. Ministry of Agriculture, Forestry and Fisheries (MAFF) 2000. Press Release No. 59: epidemiological study on the possible source of infection for foot and mouth disease outbreaks, 1 September. MAFF, Tokyo, 1 p.
5. Ministry of Agriculture, Forestry and Fisheries (MAFF) 2002. Outline of the BSE related projects for the fiscal year 2002, 5 April [in Japanese]. Agricultural Production Bureau, MAFF, Tokyo, 25 pp.
6. Ministry of Agriculture, Forestry and Fisheries (MAFF) 2003. Report on results of epidemiological analysis by the BSE Epidemiological Study Group, 30 September. MAFF, Tokyo, 99 pp.
7. Ministry of Agriculture, Forestry and Fisheries (MAFF) 2004. Report of the Highly Pathogenic Avian Influenza Infection Route Elucidation Team, 30 June. MAFF, Tokyo, 96 pp.
8. Ministry of Agriculture, Forestry and Fisheries (MAFF) 2004. Bovine spongiform encephalopathy control guidelines, 29 November. MAFF, Tokyo, 9 pp.
9. Ministry of Agriculture, Forestry and Fisheries (MAFF) 2004. Foot and mouth disease control guidelines, 1 December. MAFF, Tokyo, 17 pp.
10. Ministry of Agriculture, Forestry and Fisheries (MAFF) 2004. Highly pathogenic avian influenza control guidelines, 16 November. MAFF, Tokyo, 16 pp.
11. Ministry of Agriculture, Forestry and Fisheries (MAFF) and Ministry of Health, Labour and Welfare (MHLW) 2002. Report of the BSE Issues Investigation Committee, 5 April [in Japanese]. MAFF and MHLW, Tokyo, 70 pp.
12. Office International des Épizooties (OIE) 2004. Manual of diagnostic tests and vaccines for terrestrial animals, 5th Ed. OIE, Paris (www.oie.int/eng/normes/mmanual/A_summry.htm accessed on 27 October 2006).
13. Office International des Épizooties (OIE) 2006. Terrestrial animal health code, 14th Ed. OIE, Paris (www.oie.int/eng/normes/mcode/en_sommaire.htm accessed on 27 October 2006).
14. Sugiura K., Ogura H., Ito K., Ishikawa K., Hoshino K. & Sakamoto K. 2001. Eradication of foot and mouth disease in Japan. *Rev Sci Tech*, **20** (3), 701-713.
15. Yamakawa Y., Hagiwara K., Nohtomi K., Nakamura Y., Nishijima M., Higuchi Y., Sato Y.,

Sata T. & Expert committee for BSE diagnosis, Ministry of Health, Labour and Welfare (MHLW) 2003. Atypical proteinase K-resistant prion protein (PrPres) observed in an apparently healthy 23-month-old Holstein steer. *Jpn J Infect Dis*, **56**, 221-222.

