OIE REGIONAL MEETING ON BOVINE SPONGIFORM ENCEPHALOPATHY

Kathmandu, 26 November 2001

1. Opening session

Dr N.P. Singh Karki opened the meeting and welcomed the speakers and participants.

Dr T. Fujita of the OIE Regional Representation for Asia and the Pacific advised that the purpose of the meeting was to disseminate the latest available information on Bovine Spongiform Encephalopathy (BSE) to the member countries of the region, as preparation for anticipated increased levels of surveillance. The occurrence of two cases of BSE in Japan highlights the need for preparation for surveillance and control and for a programme of public awareness to avoid consumer panic. There is a need to secure the trust of consumers.

Dr D.D. Joshi, Chairman of the Nepal Veterinary Council, chaired the scientific session, and reaffirmed that the experience in Japan highlights the regional importance of BSE preparedness.

The addresses given by Drs Karki and Fujita, the programme and the list of participants are attached as Appendices I-IV respectively.

Dr U. Kihm, Director of the Swiss Federal Veterinary Office commenced the scientific presentations, and noted that with BSE it has been difficult to differentiate fact from fiction. The purpose of the meeting was to present the facts, to share the experiences of BSE in a number of countries and to create awareness that BSE is now a global problem. All the material presented was circulated, as a printed report and as copies of the presentations on screen (Appendices V-VI).

2. BSE globally: current situation and available tests

Dr D. Heim from the Swiss Federal Veterinary Office described the history of discoveries of transmissible spongiform encephalopathies (TSEs) and of the outbreak of BSE in the U.K. There followed a comparison of the descriptive epidemiology of BSE in the U.K. and Switzerland, and elsewhere in Europe.

Dr Heim commented particularly on the aspects of tests for BSE. Rapid tests have been validated to give clear-cut positive/negative results, but have been validated mainly on fresh specimens, not so much with autolyzed samples or samples that have been repeatedly frozen and thawed. Current tests can be applied only to dead animals, and work only towards the end of the incubation period of the disease.

Tests are best used for surveillance. Use of rapid tests for consumer protection is still a controversial issue.

Dr K. Oishi from Japan queried the possibility of a test for use on the living animal. Dr Heim advised that current research may lead to such a testing capability in the longer term but that no such test is going to be available to assist in the immediate future.

Concern was expressed by a number of delegates regarding a report of BSE in a 20-month-old animal in the U.K. It was advised that the animal was identified because it was showing clinical signs but that of over 180,000 cases only two cases were in that young age group and that these cases were detected years ago, when the load of infectivity was high. This type of rare event could be expected with normal biological variation.

Dr K. Sakamoto from Japan asked that since Japan now has had two cases what predictions could be made. Can an epidemiological study indicate how many more cases are likely?

It was replied that where there have been one case more cases follow, due to the nature of the contamination. The recommendation is to do a risk assessment on the import and distribution of infected material. For modelling of the likely progress of an outbreak at least two years of data is necessary.

Dr D. Carton of New Caledonia queried the definition of downer cows as it related to TSE surveillance. Dr R. Tanaka of the U.S.A. indicated that the purpose was simply to identify animals that may represent a higher risk cohort.

3. Surveillance and diagnosis

Dr Kihm showed a video tape of an approach to the clinical examination of cattle to detect BSE. Observations should be made of behaviour, sensitivity and locomotion.

Behavioural characteristics include alertness, excitability, sudden jerks of the whole body, fear, salivation, "bug eyed" appearance, teeth grinding, licking of the muzzle, wrinkling of the nose, muscle fasciculation, movements of the ears and recumbency.

Animals may be sensitive to touch, sound or light. To assess response to touch run the hand and then a pen or pointer over the neck, head, shoulder, along the dorsal and ventral abdomen and "broom test" the feet. To assess response to sound observe responses to metal clanging noises, such as jerking of the head or salivation. To assess sensitivity to light, restrain the animal in a dark place then shine a bright light on the head. Observe for jerking movement, muscle fasciculation or evasive actions.

Disturbances in locomotion may include walking stiffly, swaying, making small jumping movements over negligible objects, or a "string-halt" action.

Members were invited to request free copies of the video.

Clinical identification and reporting of suspect cases is an important component of surveillance, supported by laboratory confirmation or exclusion. Dr Heim gave a detailed account of the Swiss experience with passive and active surveillance.

During discussion, Dr Kihm raised the question of whether countries covered by the OIE Regional Commission for Asia, the Far East and Oceania need a regional reference laboratory. This issue should be considered now to allow discussion on planning to commence. The issue must also consider which competencies are needed by each country. Some tests are quite expensive, up to $30 per test for the new rapid tests. Histopathology is a most useful and relatively inexpensive approach, supported by immunohistochemistry.

Dr Joshi from the Chair raised the issue of whether buffaloes are susceptible. There have been cases in bison, but there is no information on bubaline species. Dr G. Murray of Australia noted that there are large populations of such buffalo in Europe and that preliminary data may be available from countries there. Europe may be able to provide advice on risk and susceptibility of bubalines that would be of use to countries in the region. Dr Heim noted that milking buffalo may not be covered by current EU regulations.

Dr Kihm recommended the use of classical surveillance based on clinical signs to remove suspect animals prior to slaughter, to help ensure that infected material does not inadvertently go for rendering. Dr Sakamoto advised that Japan is following this approach and that in a baseline study in response to the first case 4.5 million cattle in Japan have been examined clinically.

Dr Joshi noted that some countries do not have an organised slaughtering system, which raises challenges for surveillance.

It was emphasised that targeted surveillance based on risk is preferred to testing all animals at slaughter as is the case in Japan, or animals over 24 months as is the case in Europe.

4. Pathogenesis of TSEs

Dr Heim next discussed pathogenesis of TSEs, and the problems of how to detect infectivity. In BSE infected cattle, brain, spinal cord, trigeminal and dorsal root ganglia, the eyes and the ileum have certainly been shown to contain infectious material.

Dr L. Gleeson of Australia queried whether the infectious material in the ileum could represent residual ingested material trapped in gut lymphoid tissue. If so, were there implications for the feeding of meat and bone meal (MBM) to other species such as chickens? Even if such species were not susceptible, could this be a possible route of passive transmission to third susceptible hosts ingesting chicken carcasses or components?

Dr Fujita asked how prions get to the brain following ingestion of contaminated feed. This is not known; it has not been possible to trace the agent using available technology. Dr B. O'Neil from New Zealand queried whether the amounts of prion involved could be below the level of detection of tests. This was agreed, but Dr Kihm emphasised that such low levels of agent are not necessarily associated with risk of transmission.

5. Measures for the management of BSE

The objectives are to eradicate BSE in animals and to reduce human exposure. Dr Heim presented information on aspects to address, particularly the role of culling of animals, rendering conditions, ruminant feed bans, removal of specified risk materials (SRM) and total feed bans.

Dr O'Neil questioned why Swiss procedures call for removal of visible lymph and nerve tissue among the SRM but the EU did not. It was advised that the Swiss requirements were drawn up prior to those of the EU, when information was not as complete, and were more conservative and based on data relating to Scrapie infectivity.

Dr Murray noted comments that adulteration of other products such as fish meal and soya bean meal with MBM could occur. What tests are available to address this issue? Dr Heim replied that PCR was being developed, but was proving problematic to apply.

Auditing of feed bans is an important aspect of management of BSE. Incidents such as cross contamination of wheat as reported in Switzerland emphasise that even in well regulated environments problems can occur and that care must be taken in attention to detail.

Dr Murray questioned whether there was a risk of prion recycling if contaminated MBM was fed to pigs or poultry. In reply it was advised that pigs inoculated by the intracranial route could become diseased and so could not be said to be refractory to prion disease. However feeding pigs with 1 kg of infected bovine brain had not resulted in disease. In Europe surveillance of pigs has not revealed lesions of TSE. There was considered to be negligible risk of prion recycling if MBM was fed to poultry. Intracranial inoculation of chickens has shown no evidence of infection.

Dr Joshi inquired whether vaccines were being developed. It was replied that prions do not induce antibodies in natural disease. Although new research results show that in principle the development

of a vaccine could be possible, immunologically mediated prevention does not seem likely in the foreseeable future.

Dr J.B. Gurung from Bhutan inquired whether surveillance could be restricted to just the small proportion of stock that could have been fed MBM. It was suggested that the full risk assessment process be followed to increase confidence in identification of exposed and non-exposed groups in the cattle population.

Dr Kihm reminded the meeting that since 1990 MBM has been very cheap and that financial pressures could have resulted in its being used in unexpected places.

Dr S.K. Ranjan of India queried the likely explanation for BSE cases born after the feed ban. The answer lies in the level of compliance with the feed ban. There is no evidence for any route of transmission of BSE other than ingestion of contaminated feed.

Dr D. Kumar Singh of India questioned whether vaccines and biologicals could transmit BSE. Dr Heim replied that there has been one report of Scrapie being transmitted in this way so in theory it could be possible.

6. Risk assessment

The exposure in Japan was said to have derived from imports of MBM. It can be expected that other countries in the region will have a similar experience to Japan.

It is recommended that the response to this situation start immediately. This involves looking at the available information, collecting data, and commencing the process of risk assessment as outlined in the presentation. The diagnosis of a case of BSE is not a matter of blame; many countries in the world are at some risk.

Dr Joshi noted that with current trading patterns risk material from a European source could have been imported via a third country.

Dr Ranjan asked whether the international trading of MBM should be banned. Dr Kihm suggested that consideration could be given to developing new rules for trade in MBM under the animal health code. Dr Murray commented that adulteration of product as mentioned earlier is not the only problem and that cross contamination can occur where shipping on containers are used to transport different products.

7. BSE in Japan

Dr Oishi and Dr Sakamoto reported on the BSE cases in Japan.

Case 1 was a dairy cow, a Holstein, 64 months old, born on 26 March 1996 in Hokkaido. It was moved to Chiba on 8 April 1998 and had two calves. On 6 August 2001 it was diagnosed with septicaemia and slaughtered. On 15 August it was tested BSE negative by western blot, but on 24 August was diagnosed as a BSE case by histopathology. On 10 October it was confirmed BSE positive by immunohistochemistry, a result confirmed on 21 October 2001 by the U.K.

Trace back revealed that the farm of origin in Hokkaido had closed but that 24 cattle distributed from there were traced. The farm in Chiba was a dairy farm with 46 head of cattle.

The emergency measures adopted included a pathological examination of all the cattle associated with the two farms, a clinical examination of all cattle farmed in Japan, an investigation of feed sources

and feeding, a change of surveillance practices on farms and a ban on the importation and use of MBM in feed for all animals.

In the emergency examination of cohorts, 70 cattle were killed and tested by ELISA and immunohistochemistry, with negative results. An examination of the veterinary records of a further 102 animals associated with the farms revealed no suspect cases.

In the emergency examination of all cattle, 4,592,567 on 136,367 farms were examined in three weeks. No further clinical cases were detected at that time.

Feeding of MBM has been prohibited since 1996 but 5,129 cattle were identified that had been fed MBM in spite of the prohibition.

Under the new surveillance system adopted since 18 October 2001 all cattle showing CNS signs, or cattle over 24 months of age that die from any cause, are tested by ELISA. Suspect reactions are to be confirmed by western blot, histopathology and immunohistochemistry.

On 4 November a decision was made to stop the importation and use of MBM even for fertiliser.

Case 2 was diagnosed at a slaughterhouse on 21 November 2001. It was a dairy animal, a Holstein, 67 months of age, born on 4 April 1996 in Hokkaido. It had three calves. It was diagnosed as a BSE case by ELISA and confirmed by western blotting.

Dr Carton, New Caledonia, sought clarification whether every animal is tested before consumption, even calves. This was confirmed to be the case. Carcasses are held until test results become available. Specified risk materials are removed from cattle of all ages at slaughter and incinerated. Since post slaughter ELISA testing commenced in October, over 80,000 animals have been tested.

Dr Joshi thanked the Japanese presenters for their description of the incident, the risk factors identified and the control measures adopted.

8. The implications of the Japanese experience for other countries globally

Dr Kihm noted that many tons of MBM had been imported by Japan during the period of risk and that other countries would also have suffered similar exposure to a greater or lesser extent.

The recommendation to all countries is to make an active response to this situation. There is a need to look at the data and commence a risk assessment.

Dr John Edwards of the OIE Regional Coordination Unit in Bangkok raised the possibility that the high costs of test may be a problem in some countries. Dr Heim recommended testing of the targeted groups, and use of immunohistochemistry. Dr Kihm commented that histopathology by trained pathologists was a very effective diagnostic test.

9. The OIE/FAO/WHO conference on BSE

Dr B. Vallat, Director General of the OIE reported to the meeting on the key outcomes of the Joint WHO/FAO/OIE Technical Consultation on BSE: Public Health, Animal Health and Trade held in Paris on 12-14 June 2001, as circulated in the "Conclusions and Recommendations" document (Appendix VII). He reminded participants that OIE had commenced deliberations on BSE prior to 1990. It had identified a need for synchronisation with WHO and FAO. In the recent conference he was pleased to report that all three organisations had adopted the same recommendations.

During discussion, Dr Kumar Singh queried whether semen is absolutely safe. The consequences of scientific opinion on this issue being wrong are quite substantial. Dr Vallat and Dr Kihm advised that on current scientific knowledge neither milk nor semen represent any risk of transmission, on the basis of both epidemiological and experimental studies. Therefore under the principles of the WTO trade in these commodities should be allowed as outlined.

Dr Murray inquired whether revisions to the overall recommendations may be expected over the next 12 months. Dr Vallat replied that not all scientific issues have been resolved and that hence there would be revisions. One area would be the guidelines for the use of rapid screening tests.

10. Recommendations

The following recommendations were adopted:

(1) Member countries of the Regional Commission recognise that the international trade in MBM has resulted in BSE becoming a global problem. No country can assume it has not had exposure to BSE without a detailed risk assessment.

(2) Member countries undertake formal, detailed risk assessments of the possibility of cases of BSE occurring in each of their countries, giving consideration to:

- Livestock and MBM imports from Europe;
- Livestock and MBM imports from countries that may have been otherwise exposed; and
- The possibility that the BSE agent was recycled and amplified.

(3) Member countries establish as a matter of urgency a laboratory diagnostic capability for BSE based on histopathology and immunohistochemistry, in order to be able to exclude BSE as the cause of cases of neurological disease.

(4) Countries initiate a programme of targeted surveillance in risk populations and a passive surveillance system based on reporting and investigation of cases of neurological disease, including training in clinical examination techniques and submission of correct samples for laboratory examination.

(5) There should be a programme of communication of the risk assessment and risk management process and surveillance strategy to public health authorities, the media and the general public, to help maintain consumer confidence.

11. Closing remarks

Dr Joshi summarised the proceedings of the day. He thanked Dr Karki for highlighting the importance of BSE to the region. Dr Kihm and Dr Heim were thanked for their presentation of existing knowledge, especially the epidemiology and the measures taken for control. Participants were asked to seriously consider the need for surveillance. Taking the right decision at the right time is important at the policy level. A risk assessment is necessary for each country to assess its situation.

Dr Joshi continued that communication is also most important. The media may have different perspectives from the scientists and that it is important to manage this situation. With respect to diagnosis and the choice of laboratory test, again the risk assessment process will be the best guide to each country.

Japan was particularly thanked for sharing their recent experiences, particularly the details of the rapid responses.

Dr Fujita closed the meeting by again thanking all contributors and participants.