Opinion on the possible vertical transmission of Bovine spongiform encephalopathy (BSE) adopted by the Scientific Steering Committee at its meeting of 18-19 March 1999

THE QUESTION

In the light of the advice that milk is unlikely to be the route of infection in case of maternal transmission the following issues were addressed:

a) other possible routes of infection to explain maternal transmission of BSE

b) a risk assessment for these routes, and,

c) recommendations for options to mitigate the risk from these routes.

In this context the SSC addressed the question: " *What is the nature and extent of the risks of vertical transmission (to include via semen, embryos or other ways of maternal transmission) of the BSE agent between cattle or between small ruminants of the same species, based on current data?"*

DEFINITIONS USED IN THIS OPINION

Vertical transmission is defined as:

- infection of the new-born, un-suckled offspring of infected or affected individuals in the absence of any other source of infection than that in the sire or dam or,
- The inheritance of genes that, independent of the presence of infection, will result in disease in all, or a proportion, of the offspring of the present or subsequent generation or,
- A combination of these factors.

Maternal transmission is defined as transmission of infection from the dam to the offspring *in-utero* or in the immediate post-natal period.

Embryos means embryos and ova.

PrP (a noun) stands for the prion protein. ***PrP*** (adjective) means the prion protein gene.

Low. In this document we use the term low in relation to risk, understanding the imprecision of the term. However, there are few data available to enable the Scientific Steering Committee to be more exact.

ANSWER

Preliminary remarks:

1. One of the problems encountered when preparing the present opinion and the Working Group document [1] which served as its basis, was the lack of results of research on a number of issues addressed by the WG and of epidemiological studies related to the use of semen and embryos traded between countries.

With respect to basic research, the SSC therefore strongly recommends that research be started or strengthened in the fields identified by the Working Group as "deficits in knowledge". Special attention should be given to the testing of the infectivity of semen, embryos, colostrum and milk of animals of various ages, without a species barrier [2] and via the intra-cerebral route of transfer.

With respect to epidemiological studies, the Scientific Steering Committee wishes to highlight the fact that field data on the occurrence of BSE in countries that could potentially occur as a result of the import of semen or embryos from countries with BSE was not available and therefore could not be appraised. The European Commission is invited to carry out epidemiological analyses with respect to traded semen and embryos and to take them into account when considering the opinion below. The opinion may possibly need to be amended in view of the outcome of these analyses.

2. The Scientific Steering Committee considers that the formulation as such of recommendations for options to mitigate the risk from maternal transmission of BSE refers to risk management and is beyond the scope of its mandate and should be addressed by the appropriate Commission Services. The SSC has nevertheless prepared a (non exhaustive) list of elements which could be considered by the European Commission when considering the present opinion. This list is given in annex.

Taking account of current knowledge and absence of knowledge:

In regard to cattle with BSE:

In situations where there has been a high incidence of infection via feed, there is a risk of transmission from dam to offspring, by a mechanism that is not understood. In the presence of maternal preference of transmission, there may be a higher risk from material derived from the female than from the male animal. On the basis of the data currently available, the Scientific Steering Committee concludes that:

- The results of all epidemiological studies undertaken to date have been consistent with a rate of maternal risk enhancement of approximately 10% in the offspring of dams within 12 months of the onset of clinical signs of BSE. Where the time lapse between parturition and onset of clinical symptoms is longer than 12 months, the rate of maternal transmission is reduced. Whether infectivity is transferred directly before birth or after birth by a variety of mechanisms (e.g., calve infection by contaminated material, environment contaminated with blood, feces, infected feed, etc.) is uncertain and should be further investigated.
- There are no scientific data to support the hypothesis that infected calves are unduly sensitive to infection on a genetic basis.
- On the basis of the limited data available, it appears that there is no enhanced risk of the development of BSE in the offspring of sires who developed BSE. It is therefore unlikely that semen constitutes a risk-factor for BSE transmission.
- Preliminary results from the incomplete embryo transfer study suggest an extremely low risk of transmission (95% confidence limits: 0-1.5%). These results are consistent with maternal transmission being mediated later in the gestational period either during or following birth of the animal.
- transmission of BSE by artificial insemination is unlikely for semen derived from BSE-affected bulls early in their incubation period;
- transmission of BSE by *via* embryos is unlikely provided International Embryo Transfer Society (IETS) protocols are used.

As regards the risks from bovine milk, the Scientific Steering Committee refers to the continuous review by the UK Spongiform Encephalopathy Advisory Committee (SEAC). SEAC has regularly discussed the safety of bovine milk in regard to BSE, the last time on 9 November 1998. The latest substantive SEAC view, expressed on 16 April 1997, was that the measures currently in place to protect the consumer were considered appropriate. (UK law states that milk derived from BSE affected cattle or cattle suspected to have BSE shall not be sold, supplied or used for human or animal consumption, with the exception that it may be fed to the cow's own calf.) SEAC concluded then (16/4/97) that no evidence had been found to suggest that milk from any species affected by transmissible spongiform encephalopathies was infectious. The Committee is keeping the possible risk infectivity in milk under review and stated most recently on 14 May 1998 that there was no reason to change their previous advice on the safety of milk. This advice may need to be updated as new data and information become available.

However, the Scientific Steering Committee notes that, in the absence of any infectivity studies on semen, embryos, fetal tissue, milk and colostrum by i/c inoculation of the homologous species in bovines, ovines and caprines, and in the absence of all the necessary experimental and epidemiological data as detailed in the report, precise estimates of these

risks cannot be made.

In regard to cattle with scrapie:

Scrapie has not been reported as a natural disease of cattle. In regard to experimental scrapie in cattle judgement cannot be made as there are no data.

In regard to small ruminants with scrapie:

- Due to inadequate and conflicting data a judgement cannot be made on the role of semen or embryos transferred using IETS protocols. However, there is no evidence to suggest that semen presents a high risk.
- There is no biological evidence for vertical transmission by genetic means. However, there is evidence that in the presence of infection certain *PrP* genotypes can influence the incubation period in a significant way.
- Maternal transmission *via* contact with, or consumption of, placenta from infected sheep can result in exposure of the offspring to infection. If these sheep are of a susceptible *PrP* genotype they may develop disease if they live long enough. It is also possible, though unproven, that in the absence of disease such sheep could transmit scrapie to subsequent generations. Uncontrolled horizontal transmission of infection from the placenta of infected sheep is probably, overall, a more important means of spreading infection within a flock than maternal transmission.

In regard to small ruminants with BSE:

BSE has not been reported as a natural disease of small ruminants. In regard to experimental BSE in small ruminants judgement cannot be made as there are insufficient data.

***Annex*: Possible elements to be taken into consideration to mitigate the possible risks of transmission of BSE via maternal transmission routes**

The risk assessments in the preceding report take account of the worst scenario situation i.e. use of products from cattle with clinical signs of BSE and confirmed to have the disease post mortem. Measures in place in the EU or applied nationally by countries with BSE in native-born animals would reduce the risk of the vertical transmission of BSE and thus further protect animal health. Those measures which are scientifically based are recommended to be applied universally. To achieve this objective, the attention is also drawn to the elements below:

a. ensure that semen and embryos are derived from clinically healthy animals.

b. For embryos, the Scientific Steering Committee refers to the measures listed in the draft OIE Code on BSE (version of January 1999). In addition, it is recommended that embryos from healthy females, not the offspring of BSE affected females but conceived by mating with semen from bulls suspected to have BSE should not be used unless and until the bull either recovers to normality or, if slaughtered, BSE is eliminated following pathological examination of brain tissue by an approved method **.**

c. Although the OIE considers that bovine semen can be traded or imported without restriction, the Scientific Steering Committee wishes to recommend:

- Semen from bulls suspected clinically to have BSE should not be used for artificial insemination unless and until the bull either recovers to normality or, if slaughtered, BSE is eliminated following pathological examination of brain tissue by an approved method.

- A bull suspected clinically to have BSE should not be used for natural service until the suspicion of BSE is eliminated.

- Semen from bulls under 20 months [3] old need not be restricted. (Remaining stocks of) semen from bulls over 20 months old, confirmed to have BSE should be destroyed other than for use for research in projects under the control of the competent veterinary authority.

d. As a precautionary measure, milk and colostrum from cattle suspected to have BSE should be destroyed so they can enter no food or feed chain. Two exceptions can be permitted, namely that milk or colostrum may be fed to the cows own calf or they can be licensed for use for research in projects under the control of the competent veterinary authority.

e. In addition, the SSC recommends that parturient cattle clinically suspected to have BSE should be isolated in premises approved by the competent veterinary authority until at least 72 hours after parturition or until the fetal membranes have been dropped or removed, whichever is later. The fetal membranes, bedding and other contaminated waste materials should be disposed of, ideally by incineration. The isolation premises should be cleaned and disinfected using an approved disinfectant capable of inactivating the BSE agent, following vacation and before any other animal enters.

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[1] The Working Group document is available separately, also on internet, as "Report on the possible vertical transmission of Bovine Spongiform Encephalopathy", submitted to the SSC at its meeting of 18-19 March 1999.

[2] Regarding inoculating cattle i/c with milk, the following comment can be made: In practice it might prove to be more appropriate / useful to look (also) at certain fractions of milk and to use transgenic mice rather than cattle once the model is proven. The aim of the experiments should be to improve the confidence that milk and colostrum do not transmit BSE. Colostrum is more important in the context of protecting animal health and eventually eliminating BSE and thus a BSE source for humans.

[3] 20 months is the age of the youngest bovine animal so far where BSE has been diagnosed.