Possible causes and routes of transmission of BSE

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ABSTRACT: An important document based on papers and reviews addressed by members of the TSE/BSE ad hoc committee was recently released by the EC Health & Consumer Protection Directorate-General. With permission, this review reproduces the Executive Summary and the Tables of Contents from Parts I and II. Refer to the referenced web page for the complete content and citations.

Keywords: TSE, BSE, bovine spongiform encephalopathy, and similar terms

Most of information issued by European Commission,Health and Consumer Protection Directorate-General is distributed by means of an electronic bulletin CENTAURNEWSLETTER FLASH INFORMATION – CNFI to the
members of the CENTAUR network (Wojciechowski *etal*., 2001). Reports on results of testing, opinions of the SSC and remarks to EC documents related to BSE and nCJD were the subjects of 146 and 32 issues, respective-ly, distributed by e-mail CNFI since March 2000 (http://centaur.vri.cz). "Hypothesis on the Origin and Transmis-sion of BSE" is an important document published by ECrecently (Opinion, 2001). The executive summary and table of contents are published in this review with per- mission as original text.[1)]

INTRODUCTION:
EXECUTIVE SUMMARY

When preparing its opinions on BSE-risks, the Scien- tific Steering Committee (SSC) has frequently been con-fronted with the unknowns related to the 'Origin of BSE'and with 'Alternative hypotheses for the transmission'of this disease other than *via* animal proteins and mater- nal transmission. It therefore invited the TSE/BSE *ad hoc*Group to prepare two scientific reports presenting the state of affairs on both issues. At its meeting of 15 No- vember 2001 the TSE/BSE *ad hoc* Group discussed and adopted the reports which will be updated according as new firm, data-supported evidence or soundly supportedhypotheses become available.
These reports can be summarised as follows:
With regard to the origin of BSE
The origin of BSE remains unknown. Given the available data, the prion protein is central to TSE sci-ence and that MBM is the main vehicle for BSE transmission with accidental cross-contamination of ruminantrations with MBM being an important feature in perpet- uating BSE epidemics after feed bans were in place.
The origin of the BSE prion is also not known, and many hypotheses have been suggested, including *for ex-ample* an origin from mammalian species other than cat-tle (a mutant form of scrapie agent from sheep, an unmodified scrapie agent from sheep, a natural TSE in *Bovidae* or *Felidae* or other wild animals whose carcass-es were rendered into MBM, the existence of a form of sporadic BSE akin to sporadic CJD of humans, a sponta-neous mutation of normal bovine PrP into an infectious and protease resistant TSE prion, etc.). For none of thesehypotheses is there enough data to either substantiate or to reject it. To differentiate these hypotheses the crucial issue is whether the nature of the epidemic is an extend- ed common source or a point source followed by repeat-ed recycling before being recognised. Regarding the origin of BSE, both hypotheses remain open.
Disease in an extended common source epidemic occurs more or less concurrently in multiple, widely dis-persed different geographical locations that each have thesame, or similar, exposure to the same contaminating in-fection at approximately the same time. The hypothesis of an extended common source epidemic would fit with the observations that BSE appeared in most parts of GreatBritain within a short space of time, shorter than the meanincubation period of BSE and that regional differences could be explained by the epidemiological findings.
A point source epidemic is one originating from a singleton event, or focus, and then spreading from that point. An example would be importation of a bovine an-imal incubating, or affected with foot and mouth disease,but was undetected and mixed with other cattle which then became infected and dispersed the virus to other susceptible animals and species in the same or distant

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geographic locations. The discrimination between a pointsource and common source is thus not easy because a pointsource, at the end of the initial stages of spread, would take the characteristics of a common source. A point sourceepidemic is thus feasible but it would imply that in the intervening years (say 10–15 years or 2–3 incubation periods) between initial exposure and the first detected cas-es coming to light no veterinarian detected a new disease,nor was confident enough to submit a brain to a compe- tent laboratory for microscopic investigation. This is con-sidered uncertain. However, if more evidence for a point source epidemic would come forward in the future, thenmany currently rejected or partially rejected hypotheses (e.g. the BSE infectious agent could originate from any mammal susceptible to TSE) would become viable.

The report addresses the view adopted in the Horn Review dated 5 July 2001 that the unique combinationof demography (large sheep population compared to cat-tle population and large amount of sheep waste generat- ed for rendering), events (rendering changes) and particularly calf feeding practices in the UK is a plausi- ble explanation of why BSE was initiated on such a scalethere and not elsewhere. The Horn review also consid- ered that there might be an age susceptibility to BSE in- fection and that this could be investigated experimentally.

It is acknowledged, however, that other alternative hypotheses on the origin of BSE exist. Some are not sup-ported and can be rejected as not being possible to causeBSE under any condition *(e.g.* the autoimmune hypothe-sis, the bacterial *(Spiroplasma* sp.) hypothesis, the singlestranded DNA hypothesis or an origin from *Coenurus ce-rebralis*) and others are implausible and difficult to inves-tigate at the present time. Some of the latter hypotheses are related to the nature of the agent and how it causes itseffect, such as by a toxic action (e.g. fat-associated chem-ical toxins in tallow or organo-phosphorous compounds)or deficiency such as an inadequate exposure to prostag-landins). If at all, they are likely to only partially and min-imally contribute to the BSE epidemic, for example by altering susceptibility of an animal to TSE infection. Theydo not help particularly in identifying an alternative ori- gin for BSE, but they could be important to consider oncethe real nature of the agent is defined and accepted. It is therefore perhaps wisest at present to still keep an open mind on the nature of the agent and to consider rather that its structure is unknown or at least uncertain.

On BSE transmission

There is very clear and strong support from epide-miological studies, rendering studies and the effect of feedbans in all countries with BSE, for the hypothesis of in- fected mammalian protein in the form of MBM beingthe major vehicle for BSE transmission in cattle. It canenter the feed deliberately, or accidentally by cross-con-tamination. However no-one has reported so far, an ex- periment to test this hypothesis using compound feed withMBM containing the BSE agent rather then infected cattle tissues only.

The actual occurrence of cross-contamination of ruminant diets with infected mammalian protein (especially MBM), even though it is not suspected, is not con-sidered to be a possible “third way” of BSE transmission,but part of the feed route. Cross-contamination can oc- cur readily during feed preparation in feed mills, during transportation or on farm, unless stringent measures are taken to avoid it. Usually, cross-contamination would have been accidental. It is possible that the accidental “cross-contamination” route of exposure could account for the bulk of, if not all, assumed ‘Third Way’ cases.

The incorporation of infected ruminant- or mammalian-derived materials in feed other than MBM is anoth- er possibility of transmission which also is not a “third way”. Such materials might have been gelatine, fat or blood (or protein products derived from them) in which the starting materials were contaminated. Effectively en-forced SRM bans and improved and authorised ruminantstunning and processing methods (including for render- ing, and for gelatine and fat manufacture) should now eliminate such causes.

Maternal transmission is theoretically a possible route of transmission since it would appear to occur in natural scrapie in sheep. There is some statistical support for the possibility of some form of maternal transmission of BSE in cattle, but if existent it cannot accountfor more than 10% (c.i. 5–15%) of the offspring of all caseswith BSE and probably less if transmission to calves occursonly if the dam is in the late stage of BSE incubation. How-ever, there is no evidence so far that this so called ‘maternaltransmission’ occurs in the absence of a feed borne sourceand no plausible mechanism for the so-called maternal transmission has been identified.[2)] Nevertheless, it is notcurrently possible to eliminate maternal transmission completely as an occasional cause of BSE.

Any other cause than from feed or maternal transmission becomes a potential ‘Third Way’. Possible

gen- uine ‘Third Ways’ are listed and discussed in detail in the report. Some, though unproven, may increase sus- ceptibility to the disease. Many are theoretically possi- ble (e.g., environmental contamination after unauthorisedburial of carcasses of non-declared BSE cases) but, if existent, unlikely to have significantly contributed to theBSE epidemic. They may, however, initially have been overshadowed by the feed and maternal transmission routes of transmission and eventually become a factor inthe current trend of the epidemic impeding the rapid to- tal elimination of the disease.

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[2)] In sheep a plausible mechanism has been identified, *i*.e., from the placenta of infected sheep. However, comparable investigations in cattle were not conclusive.

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Full text of the 67-page opinion (adopted 29-30 November 2001) is available in PDF format at http://europa.eu.int/comm/food/fs/sc/ssc/out236_en.pdf. The committee was appointed by the European Commission's Health and Consumer Protection Directorate-General. The opinion is part of Directorate C: Scientific Opinions and C1: Follow-up and dissemination of scientific opinions. Emergency management of transboundary cattle diseases in Southern and Eastern Europe was addressed by Wojciechowski

K.J., Paskin R., Pite L., and Hruška K. in 2001. Reference: Vet Med - Czech, 46, 225-228 (http://www.vri.cz/docs/vetmed/46-7-225.pdf).

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