

SEAC 102/2

NEW RESULTS ON IDIOPATHIC BRAINSTEM NEURONAL CHROMATOLYSIS FROM THE VETERINARY LABORATORIES AGENCY

ISSUE

1. The Department for Environment, Food and Rural Affairs (Defra) has asked SEAC to consider a research article (Annex A) entitled “Idiopathic Brainstem Neuronal Chromatolysis (IBNC): a novel prion protein related disorder of cattle?” produced by the Veterinary Laboratories Agency.
2. Martin Jeffrey, the lead author of the article, will be present at the meeting to present an overview and answer questions.

BACKGROUND

3. IBNC is a rare¹ neurodegenerative disease of adult cattle. This disorder has some clinical similarity to BSE and was initially recognised from histological examination of cattle brains submitted as part of the UK surveillance for BSE diagnosis in 1989. However, the brains of IBNC-affected cattle have pathological features which are clearly different from those seen in BSE. Most cases have been detected in Scotland, but it is not known if this is a true distribution or primarily because Scottish scientists have examined BSE negative cases in more detail. The last reported case of IBNC in an animal presented as a BSE suspect was in 2005, in an animal born in 1992.

PREVIOUS CONSIDERATION BY SEAC

4. SEAC first considered IBNC at its 14th meeting (April 1993) and emphasised the importance of defining the new condition in detail with

¹ Between the years 1988 and 1991 IBNC occurred in Scotland with an incidence of 7 cases per 100,000 beef suckler cattle over the age of 6 years (from Annex A).

transmission studies and PrP examination. The next discussion was at the 19th meeting (June 1995), when the committee reflected on results of transmission studies in mice (VM, RIII, C57 and C57xVM mice) from brains of two cattle with IBNC. Some mice had shown signs of TSE disease, but it was suggested this could have been due to low level BSE contamination of the samples. The committee recommended that further investigations should be carried out on isolates from brains of IBNC cases with removal of the brain and subsequent handling under conditions that would prevent contamination.

5. At the 49th meeting (March 1998) the committee considered a further IBNC transmission study in which the brain from an IBNC case was removed under aseptic conditions. The mouse strains challenged were RIII, VM, C57BL, C57BL x VM and IM. These experiments ran for between 577 and 631 days and no clinical signs of transmission were evident. The Committee stated² it was content that, although little was known about IBNC, it did not constitute a health risk to man because suspect IBNC cases would be taken as BSE suspects or caught by the Over Thirty Months (OTM) Scheme.

6. Annex B contains the minutes of the discussions on IBNC at previous SEAC meetings.

NEW RESULTS

7. The research article “Idiopathic Brainstem Neuronal Chromatolysis (IBNC): a novel prion protein related disorder of cattle?” was published in September 2008. The cases studied concerned brains from cattle killed between 1993 and 2005 when they were between 5 and 15 years of age. All of the 15 cattle tested showed that the brains had abnormally accumulated prion protein.

8. Defra has asked that SEAC considers the VLA paper in order to confirm or revise its previous views on this disorder as:

- This is the first time IBNC has been shown to be associated with abnormal expression or accumulation of the prion protein.
- The previous transmission studies conducted in the 1990s were inconclusive and repeat studies are planned.
- IBNC is thought to be rare but the exact prevalence of the disorder is unknown, as IBNC would not be picked up through the

² At 49th SEAC meeting (9th March 1998), paragraph 52, see Annex B.

active surveillance programme for BSE which uses rapid post-mortem tests to detect proteinase-K resistant PrP^{Sc}.

9. Additionally, TSE controls on older cattle have changed since the previous SEAC advice in 1998. For example the OTM Scheme, which was in operation then, has now been replaced with testing of cattle slaughtered for human consumption aged over 48 months. Other controls remain, such as compulsory notification of suspected BSE, ante-mortem inspection, specified risk for cattle slaughtered for human consumption and a ban on cattle born or reared in UK before 1st August 1996 entering the food chain.

FUTURE RESEARCH

10. VLA are hoping to carry out further mouse transmission studies of IBNC cases as part of a larger project, on TSE molecular sciences, about which Defra is currently in advanced negotiations with VLA. If new cases of IBNC occur, it is planned that the brains from 2 cases of IBNC will be obtained and bioassayed in transgenic mouse lines, expressing bovine PrP or ovine PrP (PrP genotype AHQ), developed by the VLA.

ADVICE SOUGHT

11. The committee is asked to consider:

- if the paper changes the previous opinion of SEAC in 1998?
- if members have any comments on the further research planned?

**SEAC SECRETARIAT
FEBRUARY 2009**

ANNEX A

A copy of the paper "Idiopathic Brainstem Neuronal Chromatolysis (IBNC): a novel prion protein related disorder of cattle?"

ANNEX B

FROM MINUTES OF 14TH SEAC MEETING – 22 APRIL 1993

12. The Committee emphasised the importance of defining this new condition in detail with transmission studies and PrP examination (3 had already been examined for PrP, all negative). The total number of cases was now 50 with still only one in England.

FROM MINUTES OF 18TH SEAC MEETING – 10 FEBRUARY 1995

16. A Member told the Committee that no infectivity (by bioassay in mice) nor PrP had been found in the brains of idiopathic brainstem chromatolysis and hippocampal sclerosis cases. It is thought that the condition might be caused by a dietary deficiency, or some other metabolic disease.

FROM MINUTES OF 19TH SEAC MEETING – 21 JUNE 1995

29. A Member described the results of transmission studies in mice from brains of two cows with IBNC (paper SEAC 19/8). At the previous meeting of SEAC, and at the review of R&D, it had been announced that there was no clinical observation of a scrapie-like disease in mice: this information had proved to be incorrect for a number of reasons. Of the mice inoculated with brain tissue from the first cow, there had been mild transient clinical signs, one had shown equivocal lesions of SE but PrP studies had proved negative. From the second cow there were two definite cases of SE though the lesion distribution and incubation period were not the same as seen in mice inoculated with brain from BSE cases or any characterised strain of scrapie. The lesions in these two mice were PrP positive. There was no obvious evidence of any mix up though one possible area of cross-contamination was during the necropsy in the Perth VIC. More evidence would be needed and further transmission studies to validate the results and proposals were put forward for further study.

30. The Committee noted that the results were unusual. They questioned whether there could be coincidental BSE infection or contamination with scrapie. The Chair noted that the feeling of the Committee was that this did not represent a new agent but it was important to be prepared to say something publicly about these findings. A suggested line to take was that these were scientifically unpublishable results but in line with the policy of openness they would be made publicly available and further work done to test their validity. Since the BSE precautions were applied to IBNC cases, human health was protected. Further investigations should be carried out on isolations

from brains of IBNC cases with removal of the brain and subsequent handling under strict conditions to avoid the risk of any contamination.

31. A Member informed the Committee that the CVO had informed the CMO about the IBNC results and the transmission from retina and he, like the Committee was satisfied that the controls already in place or proposed were adequate.

FROM MINUTES OF 42ND SEAC MEETING – 23 MAY 1997

62. The Committee were advised that the paper had been circulated for information, and that no further action was proposed until further results were available unless the Committee felt otherwise. The Committee noted the paper.

FROM MINUTES OF 49TH SEAC MEETING – 9 MARCH 1998

52. The Committee had expressed concern last year that IBNC could be a transmissible disease. Mouse assays from cases had been undertaken and SEAC 49/8 was an update on information given to the Committee last year. The positive results obtained from the earlier transmission experiments were now thought probably to have been due to BSE strain 301V contamination in the laboratory. Consequently no firm conclusion could be drawn from them on whether IBNC is transmissible. The latest transmission study, had been running for between 577 and 631 days with no evidence of transmission to date. The Committee were informed that the IBNC cases had tested negative by immunohistochemistry. The Committee were content that, although little was known about IBNC, it did not constitute a health risk to man. Suspect IBNC cases would be taken as BSE suspects or caught by the Over Thirty Months Scheme.