



## **NINETIETH MEETING OF THE SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE**

The Spongiform Encephalopathy Advisory Committee held its 90<sup>th</sup> meeting in Edinburgh on 24<sup>th</sup> November 2005, and discussed the following matters:

### **CURRENT ISSUES**

SEAC was informed about the following issues:

- The SEAC Sheep Subgroup will meet on 24<sup>th</sup> January 2006 to consider emerging scientific developments on atypical scrapie and possible implications for the National Scrapie Plan (NSP) and EU TSE roadmap.
- A recent article<sup>1</sup> reporting detection of relatively low levels of abnormal prion in the mammary glands of five Italian farmed sheep with coincident clinical signs of natural scrapie and mastitis. Abnormal prion protein was absent in the mammary gland of sheep free of mastitis or scrapie. SEAC agreed that the study provided further evidence that inflammatory diseases can alter the distribution of abnormal prion protein in infected animals. However, the particular form of mastitis was rare in the UK and the sheep breed studied is prone to particular diseases. SEAC considered the study to be important. However, it would be premature to come to firm conclusions about the possible implications of the findings for UK flocks and further investigations should be undertaken. It was noted that regulations restrict milk from animals with clinical mastitis from entering the food chain.

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<sup>1</sup> Ligios *et al.* (2005) PrP<sup>Sc</sup> in mammary glands of sheep affected by scrapie and mastitis. *Nature Medicine*, 11 published online 04/11/05.

- The European Food Safety Authority recently published scientific opinions on the evaluation of rapid post mortem TSE tests for small ruminants and on classification of atypical TSE cases in small ruminants.
- The European Commission recently published a report of the Food and Veterinary Office recent inspection of BSE control and surveillance measures in Great Britain in June 2005.
- Defra had issued consultations (i) to seek views on the application of a breeding programme to reduce scrapie susceptibility in rare sheep breeds and (ii) on possible amendments to legislation to lift the EU ban on export of cattle and cattle products from the UK and on the harmonisation of UK and EU specified risk material controls.
- The Chairs of committees concerned with CJD met recently with officials from the Department of Health (DH) and Health Protection Agency (HPA) to discuss issues of mutual interest and to ensure a joined up approach was taken by the committees.
- Mr Peter Jinman (Deputy Chair of SEAC) participated in a Food Standards Agency (FSA) workshop to allow the FSA's new Chair, Dame Deirdre Hutton, to learn more about the committees that provide advice to the FSA.
- The Chair participated in a joint FSA/Royal Society workshop to discuss the possible input of social sciences into the risk assessments conducted by independent advisory committees.
- The SEAC Secretariat has begun an exercise to recruit two new specialist members to SEAC: one member with veterinary clinical expertise and one member with veterinary molecular and biochemical expertise.

## **vCJD UPDATE**

SEAC was updated on the latest figures on sCJD and vCJD cases from the National CJD Surveillance Unit. Between May 1990 and

August 2005, 788 cases of sCJD had been identified with a mean age at death of 66 (range 20-95) years. The genotype distribution of these cases was 65% MM, 17% MV and 18% VV at codon 129 of the prion protein gene. Up to October 2005, 158 vCJD cases have been reported in the UK with mean age of death of 30 (range 14-74) years. There has been no significant shift in the mean age of death of vCJD cases since the start of the epidemic; the reason for this is uncertain. All of the 134 UK vCJD cases tested to date are of the MM genotype. Elsewhere in the world, 27 vCJD cases have been reported: 15 in France, 3 in the Republic of Ireland, 2 in the USA and single cases in Italy, Canada, Saudi Arabia, Japan, Netherlands, Spain and Portugal. For one Irish case, the Japanese, Canadian and both USA cases, infection was likely to have occurred in the UK.

Statistical analysis of the UK incidence of vCJD deaths indicates the epidemic reached a peak at about 6 deaths per quarter in mid-2000 and has been in decline since then. However, a small increase in the number of onsets of vCJD had been noted in 2004 but it was unclear whether this increase was meaningful. These cases appear similar to previous cases in terms of genotype and clinical symptoms.

The committee was informed about investigations into the biochemical signature of the prion protein in samples from sCJD and vCJD cases. These analyses suggest that more than one form of abnormal prion protein might be present in the same sample. These findings suggest that the relationship between abnormal prion protein form and TSE strain is more complex than previously thought.

## **SEAC EPIDEMIOLOGY SUBGROUP STATEMENT**

SEAC welcomed and endorsed a position statement produced by the SEAC Epidemiology Subgroup in response to the committee's request for a consideration of the nature and future profile of the vCJD epidemic. The committee agreed that better ascertainment of the prevalence of infection was vital. Further consideration on how this might be best progressed was very important, and would be followed up with some urgency.

## **BARB CASE CLUSTERS**

SEAC was informed that up to 20 November 2005, 114 BSE cases born after the reinforced feed ban in August 1996 (BARB cases) had been identified in GB. Analysis suggests there is a decline in the risk of BSE infection for successive birth cohorts such that the BARB epidemic is unlikely to be sustained by animals born after 31 July 2000. Clusters of BARB cases within herds had been identified (4 pairs, 2 triplets and 1 quadruplet). Farm investigations of these clusters suggested that the feed the animals may have received when young could have been contaminated by old residual feed in storage bins. SEAC noted that advice to farmers is being formulated to remove this potential risk factor.

## **EVOLUTION OF THE PRION PROTEIN GENE**

SEAC considered a recent report<sup>2</sup> on a theoretical investigation of the molecular evolution of the prion protein gene (PRNP) in ruminants. This suggested that evolutionary selection pressures may act to maintain variation in the sheep gene, in contrast to the NSP, which is reducing variation in PRNP to select genotypes more resistant to scrapie.

SEAC considered that, although the methodology used was sound, the conclusions were not as robust as claimed. This would be followed up by the SEAC Sheep Subgroup. It was noted that Defra had commissioned a semen bank to preserve existing prion protein gene variation as well as a project to examine the potential relationship between PRNP genotype and fitness and production traits.

## **HORIZON SCANNING**

The committee was informed by representatives from DH, FSA and Defra about issues that might require future consideration by SEAC, including:

- estimation of the size of the vCJD epidemic, minimisation of the risks of secondary transmission of vCJD (DH).
- development of in life diagnostic tests for TSEs (DH, Defra and FSA).

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<sup>2</sup> Slate (2005) Molecular evolution of the sheep prion protein gene. *Proc. R. Soc. B.* 272, 2337-2344.

- relaxation of TSE control measures and the scope of TSE surveillance (Defra and FSA).

## **PUBLIC QUESTION AND ANSWER SESSION**

The Committee answered questions from the public relating to the work of SEAC. These included questions about the implications of the apparent decline in the number of suspected cases of CJD reported in the UK in recent years, the potential of magnetic resonance imaging to detect CJD before the onset of clinical symptoms and the progress of the FatePride environmental study on TSEs.

## **vCJD INFECTIVITY IN BLOOD**

The National Blood Service asked SEAC to review, in light of new information, the key underpinning assumptions made in an assessment of transmission risks via blood transfusion that SEAC had accepted in 2002. The item was discussed in the reserved business session as it involved consideration of unpublished research.

SEAC noted that new data supported assumptions made about the potential for blood from infected but asymptomatic individuals to be infectious and the susceptibility of non-MM PRNP codon 129 genotypes to infection. However, there were very few new data to inform estimates of infectivity levels in blood, the possible change in infectivity levels in blood over the course of the incubation period and the distribution of infectivity in blood components. The committee noted that robust research in these areas was lacking.

## **TSE STUDIES IN MOUSE MODELS**

SEAC considered findings from studies using transgenic mice on human to human vCJD transmission, and also the relationship between infectivity levels and concentrations of abnormal prion protein in the brain of animals with TSEs. These issues were discussed in a reserved business session to allow consideration of unpublished research.

SEAC agreed that the characteristics of transgenic models of TSE infections must be carefully considered when assessing the

implications of research using such models. The committee noted that the new research suggests there is no clear correlation between abnormal prion protein concentrations and the titre of TSE infectivity in some animal models. Thus, abnormal prion protein may not always be a good surrogate marker for infectivity. The implication of this finding for rapid diagnostic TSE tests should be considered. The committee considered that the precise role of abnormal prion protein in relation to the infectious and neurodegenerative properties of TSE agents remains unclear.