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HOUNDS SURVEY

SEAC 19/7

At its discussion in August, the SEAC asked for a re-evaluation of the pathology material in the Hounds Survey which was submitted to the Committee in document SEAC 16/4. The attached paper has been prepared as a research proposal by Mr Wells at the Central Veterinary Laboratory. It refers to possible ways in which this work could be taken forward. The question of immunohistochemistry is discussed in paragraph 3 where it is concluded that the absence of a positive control makes interpretation of the results problematic. In the view of the Department the best way of carrying this work forward if it is felt to be of sufficiently high priority would be the transmission experiments discussed in paragraph 4 of the note. However the Department would draw the Committee's attention to the fact that such experiments are expensive and that resources to do these experiments are limited. Paragraph 6 of the minutes of the meeting of 10 February deals with this issue and the question of prioritisation of candidates for transmission studies. Material from dogs does not appear in that list but clearly the Committee might wish to take a view as to whether it should and if so, what priority to give to it in relation to the other candidates for this work. It might therefore be useful if this item were discussed in the context of the overall question of priorities for transmission studies rather than in isolation. Since 2 November 1994, when the Spongiform Encephalopathy (Miscellaneous Amendments) Order 1994 came into force, all suspected cases of spongiform encephalopathy in animals and poultry were made notifiable. There is therefore now a requirement for veterinarians to report any suspect SE in canines for further investigation. None have been reported.

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IN CONFIDENCE

CONCEPT NOTE FOR FURTHER STUDY OF MATERIAL OBTAINED IN A SURVEY OF HOUNDS FOR EVIDENCE OF A SCRAPIE-LIKE SPONGIFORM ENCEPHALOPATHY (SE)

Background

The full background and results of the primary study of culled hounds, resulting from a Tyrrell Committee recommendation that the health of animal species fed bovine products should be monitored, is contained in a report by R J Higgins VIC Thirsk (March 1992).

It was established that in the dogs studied there was no evidence of a pathologically overt SE similar to that reported in the domestic cat. However, any confidence with which this lack of evidence can be accepted as an indication of the absence of SE infection, or covert disease, in the population is diminished by certain limitations in the protocol of the study. Furthermore there were certain observations resulting from the study which were uninterpretable.

These related to both the histopathological observations and the examinations for SAF:

a) The histopathological examination was uninterpretable because of post-mortem changes and damage to the brains in 10% of cases (Total examined : 444).

   Histopathological observations made in 35% of cases were unresolvable because of sub-optimal preservation of the tissue and/or localised vacuolar changes of unknown significance. The remaining 55% of brains were considered to have no significant vacuolar changes.

b) Fibrillar material closely similar to SAF, found in BSE/scrapie, was observed in 19 (4.3%) cases, all of which were hounds > 7 years of age. 14/19 of these suspected SAF results correlated with cases in the unresolveable histopathological category.

As discussed in the report the approaches used imposed the following limitations:

1. The study was inadequately controlled.

2. The dogs were not subjected to a systematic necropsy examination and only the brain, not the entire CNS, was examined histopathologically.

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3. Preservation of material was sub-optimal for critical histopathological assessment.

4. Clinical histories were not obtained and clinical examinations were not performed.

5. The sample from the population targetted for study was not entirely appropriate to seek evidence of an advanced stage of an SE.

6. Absence of a literature search and review of neurological disorders of dogs (particularly hounds) prior to the study prevented approaches to rule-out confounding lesions due to possible differential diagnoses.

The following proposals address the hypothesis that the hound survey observations represent a PrP related or scrapie-like disease of dogs in which the pathological response, and possibly the spread of infectivity, is neuroanatomically localised. By inference this could also mean that the disorder is clinically silent and non-progressive.

Approaches:-

1. Obtain further opinions on the histopathological changes in unresolved cases from veterinary neuropathologists with considerable experience of canine neuropathology.

   Potential benefit: Clearer understanding of whether the changes are consistent more with artefact than authentic pathology. Probable outcome is that observations will remain unresolved.

2. PrP genotyping of hounds (from fixed material) to attempt segregation of three coded groups of brains defined in the survey:

   A : ? SAF/histopath. unresolved
   B : ? SAF/histopath. negative
   C : SAF negative/histopath. negative

   Potential benefit: Possible identification of a "susceptible" genotype segregating with group A and possibly B. As there is no fresh material remaining from group A difficulties can be anticipated in attempting to use fixed material, from which recovery of DNA is suboptimal. It is assumed for costing that amplification of whole coding region of canine PrP gene prior to sequencing can be achieved.

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3. Immunohistochemical examination of medulla sections from coded groups as at 2 above for PrP.

Potential benefit: Colocalisation of disease specific PrP with vacuolar changes in sections from group A using a selected panel of antibodies to PrP.

Medium term study, involving immunohistochemical titration of three selected antibodies, resolution of potential technical problems operating in a different species from previous work, and investigation to clarify specificity problems arising with immunolabelling. Assumes that at least one of the 3 antibodies proves to label canine PrP^{SC}. Absence of positive control material is problematic in interpretation.

4. Transmission attempts from pools of material based on groups (A-C) at 2 above by multiple parenteral routes of inoculation (including i.c.) using two species:-

4.1 Beagle dogs (transmission without species barrier).

Potentially at least a 7 year study in dogs. Such animal work would probably be sub-contracted by CVL.

4.2 Standard inbred mice: three groups of 20 mice for each of two mouse strains (RIII and IM) (transmission with species barrier). Difficulties could be presented because material is potentially very low titre and this could be further reduced by the need to use formalin-fixed material.

It cannot be expected that any of these studies would necessarily provide definitive data on the occurrence of a scrapie-like disorder in dogs. If it were considered necessary to readdress the question of possible occurrence of such disease in the UK dog population approaches involving active epidemiological monitoring would be necessary. This naturally remains as an option. Similarly the question of the susceptibility of the species to BSE or scrapie could also be addressed experimentally as it had been for other species exposed to bovine products.

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