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BSE Standing Committee - Dr C Gibbs
12/13 March 1990

BSE file

Firstly, a welcome was given by Dr W A Watson. An introduction to BSE was given by Mr R Bradley and Dr K J MacOwan. Mr Bradley acknowledged the great contribution made to the field fo Scrapie by Dr W Hadlow. Mr Bradley also discussed the media interest in BSE some of which is adverse. Dr MacOwan discussed the funding of BSE research.

Epidemiology/Offspring - Mr J W Wilesmith

A stepwise increase in the incidence of BSE may be caused by the recycling of BSE-affected cattle back into the cattle food chain. If this is so, a further increase may be anticipated. Since 100 per cent compensation has been announced there has been an increase in the reporting of BSE suspect cases. There is a much higher incidence of the disease in South-east England and a very low incidence in Scotland. Studies in progress at present are:

1. Descriptive analysis already published.
2. Simulation modelling to assess the likely incidence of the disease in future.
3. Case control study to assess if meat and bone meal is the source of the epidemic and to investigate the geographical risk.
4. Offspring study to assess whether BSE can be transmitted maternally.

A summary of current thinking on the cause of the epidemic was given, ie. that BSE is a new disease caused by exposure of cattle to a scrapie-like agent in meat and bone meal commencing in 1981/82. A discussion followed on the husbandry of British cattle, the lack of any change in pathology or clinical signs during the outbreak and the possibility of stating BSE risks for certain British products for export.

Control and Exports - Dr D Matthews

A history of legislation and publications connected with BSE was given. BSE was first confirmed in November 1986 and made notifiable on June 21, 1988. Ruminant-derived protein was banned from ruminant feed from July 18, 1988. A slaughter and compensation policy started on August 8, 1988 and certain bovine offals were banned from being used for human consumption in November 1989. In February 1990 100 per cent compensation was awarded. During this time period scientific papers were published on the transmission of BSE to mice and cattle and two advisory committees published their reports, namely the Southwood Report and the Tyrrell Report. Some countries have imposed a total embargo on the exports of livestock from Britain and some other countries require additional certification.

A discussion followed on the rendering process and the point was made that offals covered by the ban can go into animal feeds for non-ruminants.

Transmission and CVL molecular studies - Mr M Dawson

Four cases of natural BSE from widely separated herds in England were used for transmission studies. Recipients were either Holstein/Friesian or Jersey cattle and they were challenged intravenously and by injection into

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he rostral brainstem. All challenged animals have gone down with BSE and there is a very constant period between challenge and diagnosis of between 520 to 610 days. The clinical signs were identical to the natural disease with the possible exception that Jerseys may have more forelimb ataxia. Two animals developed clinical signs rapidly after sustaining fractures. In 22 BSE-affected brains, scrapie associated fibril detection was successfull in almost 100 per cent of cases in certain brain areas such as the basal nuclei, mid brain and medulla. A discussion followed of waste disposal which is incinerated, and oral transmission experiments which have been initiated looking at transmission via placenta to calves orally but no experiments have been initiated as yet to assess whether brain can transmit BSE orally.

Pathology - Mr G A H Wells

In BSE neuropil vacuolation is a more prominant feature of the pathology as compared to Scrapie where neuronal vacuolation is more prominant. Neuronal vacuolation and astrocytic reaction also occur in BSE. A full account of the distribution of lesions was given. The spinal tract nucleus of the trigeminal nerve and the nucleus of the solitary tract are invariably involved and using these areas 99.6 per cent diagnostic accuracy is obtained for routine use for the diagnosis of BSE. There is good correlation of vacuolation to scrapie-associated fibril score in brain stem areas but this is poorer in cortical areas. Amyloid plaques are only a rare feature of BSE pathology but PrP immunostaining shows definite differences from control animals. Spongiform encephalopathies also occur in exotic ruminants. A discussion ensued in which it was stated that the neuro-pathology is not always well correlated in severity to the clinical signs but that the neuropathology in experimental cases was similar to that seen in field cases.

Mouse, Sheep, Goat Studies - Dr H Fraser

The mouse can be used as a typing system for strains of the agent. Strain typing may or may not indicate the origin of infection. The same three strains have been isolated from many different scrapie sources namely ME7, 87A and 87V. In an attempt to type the BSE agent the same four BSE cases as previously discussed were used. Two surprising things came out of these results. Firstly, the rapidity with which mice went down with the disease which in some cases was considerably shorter than scrapie. Secondly, there were differences between strains of mice which had the same genotype at the S7/P7 locus which controls scrapie incubation period. This implied that there might be another gene controlling incubation period for BSE in mice. It was a serious omission that mice which had the genotype S7/P7 were not challenged with the BSE agent because in sheep this F1 generation gives intermediate incubation periods between S7 and P7 homozygotes. Upon sub-passage from S7 homozygote mice unusually short incubation periods were seen. An account of the pathology of BSE in mice was given such as neuropil vacuolation, amyloid, PrP immunostaining and asymmetrical pathology. A discussion followed in which the bioassay was explained and Dr Fraser suggested that the particularly short incubation periods were due to the selection of a rapidly replicating mutant. The species barrier and the differences between intraperitoneal and intracerebral challenge were also discussed.

human spongiform encephalopathies and BSE - R Ridley and H Baker

From a family with the autosomal dominant Gerstmann-Straussler Syndrome (GSS) transmission to primates was successful in two members and failed in two other members of the family. Because this disease is not always transmissible or spongiform, PrP diseases has been adopted as an appellation. Alterations in the PrP gene have now been seen in a wide variety of bizarre dementures. Three hypotheses to explain the familial genetic and sporadic nature of these diseases were explained together with problems which theory encountered. The various alterations in the PrP gene seen in some of these diseases was explained. An account of the age of onset and length of the course of disease for the human spongiform encephalopathies was given. The opinion was expressed that most human cases of spongiform encephalopathys are not caught, but are familial neuro-degenerative diseases transmissible in certain circumstances. The pathogenesis of these dieseases was compared to Alzheimers disease at a molecular level. Alterations in the PrP gene may increase the probability of altered PrP being formed from the normal host protein. A discussion followed in which it was stated that the increased incidence of PrP related diseases is due to an increased awareness of these diseases and not due to BSE. Professor Gajdusek also discussed the nucleation of amyloid as a model for these diseases.

Molecular chemistry and genetics - Dr J Hope

PrP is a normal host protein and in BSE and scrapie an abnormality in this protein causes its accumulation and relative protease resistance. Messenger RNA for the PrP protein in ruminants is twice the size of that in rodents and man. Differences in PrP genes are linked to differences in the incidence and incubation of these diseases. In sheep the sip-gene affects the incubation period for scrapie and this can be detected by classical genetics and by restriction fragment length polymorphism analysis of DNA in the region of the PrP gene. Altered PrP can be detected in the spleen of a mouse terminally affected with scrapaie but PrP is only relatively protease resistant. A discussion followed about proteinase K treatment of the PrP the site of action of sip and the possibility of asymptomatic carriers of scrapie.

Inactivation studies - Dr D Taylor

Various groups are concerned about the inactivation of the BSE and scrapie agents. This group includes farmers, vets, the food industry, the renderers, medicinal product manufacturers and the general public. In the 1930s scrapie was transmitted in louping ill vaccine and in 1977 Creutzfeldt-Jakob disease was transmitted via brain electrodes. Both these occurrences were due to inactivation of the agent. Hypochlorite needs a very long time and a very high concentration to inactivate the agent. The use of sodium hydroxide needs further clarification and paracetic acid or phenolic disinfectant are not very effective methods of inactivation. Autoclaving is effective if used at a high enough temperature for a sufficient length of time but dry heat will not inactivate the agent at 160°C for 24 hours. Some strains of the agent are more thermostable than other agents such as the 22A. As regards BSE it would appear that we are dealing with a single strain only. A discussion followed on inactivation. It was stated that formic acid is effective if only used for 15 minutes and this treatment does not adversely affect pathological examination, whereas a temperature of 270°C does not inactivate formlin fixed material. Various

ier techniques were discussed and it was stated that some previous transmission experiments may have been adversely affected by contaminated instruments.

Embryo Transfer - Miss K Brown

Embryo transfer is the safest way of moving the full genetic complement of an animal without running the risk of disease. The embryo must be in a pre-implant stage with zona pellucida which is intact, free from cracks and debris. Embryos are washed 10 times with 100 fold dilution taking place each time. This procedure removes a number of organisms. The objective of the experiment is to determine whether BSE derived embryos can infect the recipient or her progeny. Donors are BSE affected field cases and recipients are imported New Zealand heifers. The donors will be super-ovulated, embryos collected non-surgically and implanted into recipients who will be kept for 7 years. Implanted embryos may be ++ using BSE affected bull semen or +- using New Zealand bull semen or pre 1980 semen. Transmission studies will also be undertaken. Unfertilised and fertilised embryos flushing media and washing media will all be separately inoculated intracerebally into mice to assess transmissibility. Many precautions will have to be taken throughout the course of the experiment to ensure that the experimental animals are not exposed to BSE from other sources by the contact with people, other animals, equipment, through food or biological products. It is possible that difficulties may be encountered with super-ovulating BSE affected animals, for example, they may stop cycling. One thousand embryos will be needed in all and 550 heifers are being imported as recipients from New Zealand. A discussion followed in which it was explained that whilst W Foote in America used surgical collection of embryos in his work with sheep scrapie this was not necessary in cattle. It was also explained that whilst it was feasible that in the early stages of the disease, a viraemia might infect the uterine tract to a greater degree, it was irrelevant because it was not possible to detect animals which would go on to develop BSE.

This report was written by Mr Iain S McGill.