The BSE Inquiry / Statement No 324

Dr James Kirkwood

(not scheduled to give oral evidence)

Statement to the BSE Inquiry

James K Kirkwood BVSc PhD FIBiol MRCVS

[This witness has not been asked to give oral evidence in Phase 1 of the Inquiry]

1. I became involved in the field of TSEs through my work as Head of the Veterinary Science Group at the Zoological Society of London’s Institute of Zoology. I held this post from November 1984 until June 1996, when I took up my present post at UFAW. During this time, concurrent with the BSE epidemic, cases of scrapie-like spongiform encephalopathies occurred in animals at the Zoological Society of London’s collections at Regent’s Park and Whipsnade and in other zoos. It was appropriate to investigate the epidemiology of these cases in order to try to determine the possible impact on zoo animals and breeding programmes, and to consider how the disease in zoo animals might be controlled.

2. Throughout the period from 1985 to March 1996, I worked at the Institute of Zoology (IoZ). I was Head of the Veterinary Science Group of the IoZ and Senior Veterinary Officer of the Zoological Society of London (ZSL). I was responsible for the provision of the veterinary service for the ZSL collections.

3. During the period from 1985 to March 1996, scrapie-like spongiform encephalopathies were diagnosed in the following animals which died, or were euthanased, at London Zoo and Whipsnade:

<table>
<thead>
<tr>
<th>Animal</th>
<th>Sex</th>
<th>Date of Death</th>
<th>Age (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arabian Oryx</td>
<td>Oryx leucoryx</td>
<td>F</td>
<td>24.3.89</td>
</tr>
<tr>
<td>Greater kudu</td>
<td>Tragelaphus strepsiceros (Linda)</td>
<td>F</td>
<td>18.8.89</td>
</tr>
<tr>
<td>Greater kudu</td>
<td>(Karla)</td>
<td>F</td>
<td>13.11.90</td>
</tr>
<tr>
<td>Greater kudu</td>
<td>(Kaz)</td>
<td>M</td>
<td>6.6.91</td>
</tr>
<tr>
<td>Greater kudu</td>
<td>(Bambi)</td>
<td>M</td>
<td>24.10.91</td>
</tr>
<tr>
<td>Greater kudu</td>
<td>(346/90)</td>
<td>M</td>
<td>26.2.92</td>
</tr>
<tr>
<td>Greater kudu</td>
<td>(324/90)</td>
<td>F</td>
<td>22.11.92</td>
</tr>
<tr>
<td>Cheetah</td>
<td>Acinonyx jubatus</td>
<td>(Michelle)</td>
<td>F</td>
</tr>
</tbody>
</table>

All these cases were described in papers published in the scientific literature (as cited below).
4. All the animals listed above were bred in captivity. The greater kudu were from a highly-inbred group whose founders were Koo (imported from West Africa in 1967), Doo (imported from a Danish Zoo in 1969) and Chester (transferred to London from Chester Zoo in 1982). The family tree of the group is shown in: Kirkwood, J.K., Cunningham, A.A., Wells, G.A.H., Wilesmith, J.W. & Barnett, J.E.F. (1993) Spongiform encephalopathy in a herd of Greater kudu *Tragelaphus strepsiceros*: epidemiological observations. Veterinary Record 133, 360-364: (J/VR/133/360).

5. The first case diagnosed among the ZSL’s animals was in the greater kudu ‘Linda’, which died in August 1989. Retrospective examination of the brain of the Arabian oryx that had died 5 months earlier, revealed that this animal also had brain lesions characteristic of a scrapie-like spongiform encephalopathy. Diagnostic histopathology of these (and of all the other cases that occurred at London and Whipsnade) was undertaken by the Central Veterinary Laboratory. The clinical features, diagnosis and possible aetiology of these first two ZSL cases was discussed in a paper published in 1990 (Kirkwood, J.K., Wells, G.A.H., Wilesmith, J.W., Cunningham, A.A. & Jackson, S.I. (1990) Spongiform encephalopathy in an Arabian oryx *Oryx leucoryx* and a greater kudu *Tragelaphus strepsiceros*. Veterinary Record 127, 418-420: (J/VR/127/418)). We noted, in this paper, that it seemed probable that these cases had a common aetiology with BSE.

6. A greater kudu ‘Frances’ which had died some 18 months earlier (17.11.87) had shown clinical signs which, in retrospect, could have been due to SE but CNS tissue had not been saved for examination so this could not be checked (Kirkwood, J.K., Cunningham, A.A., Wells, G.A.H., Wilesmith, J.W. & Barnett, J.E.F. (1993) Spongiform encephalopathy in a herd of Greater kudu *Tragelaphus strepsiceros*: epidemiological observations. Veterinary Record 133, 360-364: (J/VR/133/360)).

7. During the following 3 years, SE was diagnosed in 5 further greater kudu in the ZSL collections (see list in point 3 above). The second confirmed case in a greater kudu occurred in the 19-month old calf (Karla) born to the first confirmed case (Linda). This case gave us concern since the calf was born after the July 1988 ban on inclusion of ruminant derived protein in ruminant feeds and it was considered to be extremely unlikely that this animal could have been exposed to contaminated feeds (the kudu diet prior to February 1987 had included a cattle pellet but pelleted diets fed from then on were thought not to contain RDP). We speculated that maternal transmission may have occurred (Kirkwood, J.K., Wells, G.A.H., Cunningham, A.A., Jackson, S.I., Scott, A.C., Dawson, M. & Wilesmith, J.W. (1992). Scrapie-like encephalopathy in greater kudu (*Tragelaphus strepsiceros*) which had not been fed on ruminant-derived protein. Veterinary Record 130, 365-367: (J/VR/130/365)).

8. Since the next three animals in which the disease was confirmed (Kaz, Bambi and 346/90) were not thought to have been exposed to contaminated feeds, and were not born to dams who had been clinical cases (Cunningham, A.A., Wells, G.A.H., Scott, A.C., Kirkwood, J.K. & Barnett, J.E.F. (1993) Transmissible spongiform encephalopathy in greater kudu (*Tragelaphus strepsiceros*). Veterinary Record 132, 68), we considered the possibility that horizontal transmission may have occurred (Kirkwood, J.K., Cunningham, A.A., Wells, G.A.H., Wilesmith, J.W. & Barnett, J.E.F. (1993) Spongiform encephalopathy in a herd of Greater kudu *Tragelaphus strepsiceros*: epidemiological observations. Veterinary Record 133, 360-364: (J/VR/132/68)). The occurrence of SE in a greater kudu (324/90), that had been born in another zoo and was not thought to have been exposed to feeds contaminated with RDP, 27 months after being introduced to the group at Regent’s Park, was further cause for concern that transmission may have occurred between animals (Kirkwood, J.K., Cunningham, A.A., Austin, A.R., Wells, G.A.H & Sainsbury, A.W. (1994) Spongiform encephalopathy in a Greater kudu *Tragelaphus strepsiceros* introduced into an affected group. Veterinary Record 134, 167-168: (J/VR/134/167)).

9. At that time, around 1993, the most likely explanation of the pattern of events seemed to be that the disease in kudu was the same as that in cattle: that it had originally entered the group in contaminated feed but that thereafter transmission may have occurred between individuals (Cunningham, A.A., Wells, G.A.H., Scott, A.C., Kirkwood, J.K. & Barnett, J.E.F. (1993) Transmissible spongiform encephalopathy in greater kudu (*Tragelaphus strepsiceros*). Veterinary Record 132, 68). In view of this and the
likelihood that individuals of a wide range of species of zoo animals had been exposed we recommended (Kirkwood, J.K., Cunningham, A.A., Wells, G.A.H., Wilesmith, J.W. & Barnett, J.E.F. (1993) Spongiform encephalopathy in a herd of Greater kudu Tragelaphus strepsiceros: epidemiological observations. Veterinary Record 133, 360-364 ) that all zoo animals that may have been exposed to contaminated feeds should be observed closely and that because of the potentially serious implications for captive breeding programmes, well-described by my colleague Mr Andrew Cunningham (Cunningham, A.A. (1991) Bovine spongiform encephalopathy and British Zoos. Journal of Zoo and Wildlife Medicine 11, 605-634: J/ZWM/11/605), there was a need for caution about exporting such animals. In addition the kudu were kept isolated from other zoo animals. A very cautious approach was taken and the keeper staff used separate tools for cleaning out the kudu dens and paddocks, changed overalls and boots, used latex gloves, and, for a period until it seemed (for reasons mentioned below) less likely that the situation in kudu differed from that in cattle, collected wastes for incineration. Management practices were reviewed again in March 1996 when it was announced that cases of new variant CJD had occurred which might be related to the BSE agent. In order to pre-empt any public concern that might follow this announcement, the walkways past the kudu paddock were closed to the public. No cases have occurred in the kudu group since 1992.

10. The case of SE in a cheetah that occurred during the period, involved a 7 year-old female which had been born and lived all her life at Whipsnade (except for the final stages when she was moved to the Animal Hospital at Regent’s Park for diagnosis and treatment). This animal, which died in December 1993, had been fed on cuts of meat and bone from carcases of cattle unfit for human consumption and it was thought likely that she had been exposed to spinal cord (Kirkwood, J.K., Cunningham, A.A., Flach, E.J., Thornton, S.M. & Wells, G.A.H. (1995) Spongiform encephalopathy in another captive cheetah (Acinonyx jubatus): evidence for variation in susceptibility or incubation periods between species. Journal of Zoo and Wildlife Medicine 26, 577-582: J/ZWM/26/577).

11. During the period we also collated information on cases of SE that occurred in wild animals at or from other zoos in the British Isles. The total number of cases of which I was aware in June 1996, when I presented a review on occurrence of spongiform encephalopathies in zoo animals (at the Royal College of Pathologists’ Symposium on Transmitting prions: BSE, CJD, and other TSEs, The Royal Society, London, 4th July 1996), was 25, involving 10 species. The animals involved were all from the families Bovidae and Felidae, and comprised: 1 Nyala Tragelaphus angasi, 5 Eland Taurotragus oryx, 6 greater kudu Tragelaphus strepsiceros, 1 Gemsbok Oryx gazella, 1 Arabian oryx Oryx leucoryx, 1 Scimitar-horned oryx Oryx dammah, 4 Cheetah Acinonyx jubatus, 3 Puma Felis concolor 2 Ocelot Felis pardalis, and 1 Tiger Panthera tigris. (A spongiform encephalopathy, which was thought probably to have a different aetiology, had also been reported in 3 ostriches Struthio camelus in Germany). This list did not include cases of BSE in domesticated species in zoos (ie BSE in Ankole or other cattle, or SEs, assumed to be scrapie, in mouflon sheep Ovis musimon).

12. Since the time the above statistics were published, a few further cases have occurred in animals at or from zoos in the British Isles. The total number of cases in cheetah that have now been documented has, as far as I am aware, risen to seven (Vitaud, C., Flach, E.J., Thornton, S.M. & Capello, R. (1998) Clinical observations on four cases of feline spongiform encephalopathy in cheetahs (Acinonyx jubatus). Proceedings of the European Association of Zoo and Wildlife Veterinarians, Chester, UK, 21st-24th May 1998. Pp 133-138). There has also been a case in a bison.

13. Epidemiological aspects of the majority of these cases (those diagnosed up to the end of 1993) were considered in paper published in 1994 (Kirkwood, J.K. & Cunningham, A.A. (1994) Epidemiological observations on spongiform encephalopathies in captive wild animals in the British Isles.
Veterinary Record 135, 296-303: J/VR/135/296.) This paper was based on a paper presented at the Consultation on BSE with the Scientific Veterinary Committee of the Commission of the European Communities held in Brussels, 14-15th September 1993 (Kirkwood, J.K. & Cunningham, A.A. (1993) Spongiform encephalopathy in captive wild animals in Britain: epidemiological observations. In R. Bradley & B Marchant (Eds) Transmissible spongiform encephalopathies. Proceedings of a Consultation on BSE with the Scientific Veterinary Committee of the Commission of the European Communities, 14-15 September 1993, Brussels. European Commission. Pp 29-47: M9 tab 46). It was thought likely that at least some, and probably all, of the cases in zoo animals were caused by the BSE agent. Strong support for this hypothesis came from the findings of Bruce and others (1994) (Bruce, M.E., Chree, A., McConnell, I., Foster, J., Pearson, G. & Fraser, H. (1994) Transmission of bovine spongiform encephalopathy and scrapie to mice: strain variation and species barrier. Philosophical Transactions of the Royal Society B 343, 405-411: J/PTRSL/343/405), who demonstrated that the pattern of variation in incubation period and lesion profile in six strains of mice inoculated with brain homogenates from an affected kudu and the nyala, was similar to that seen when this panel of mouse strains was inoculated with brain from cattle with BSE. The affected zoo bovids were all from herds that were exposed to feeds that were likely to have contained contaminated ruminant-derived protein and the zoo felids had been exposed, if only occasionally in some cases, to tissues from cattle unfit for human consumption.

14. Among the affected bovids were others (including scimitar horned oryx and eland) which, like some of the kudu, were born some considerable time after the July 1988 ban on inclusion of RDP in ruminant feeds (Kirkwood, J.K. & Cunningham, A.A. (1994) Epidemiological observations on spongiform encephalopathies in captive wild animals in the British Isles. Veterinary Record 135, 296-303: J/VR/135/296). The source of infection to these animals was puzzling. However, as it emerged that many cases of BSE were continuing to occur in domestic cattle born after the July 1988 ban on inclusion of RDP in ruminant feeds, it was clear that the ban had not been immediately effective, and it was therefore possible (or, at least, impossible to rule out) that the late cases in zoo ungulates were also due to exposure to contaminated feeds.

15. We drew attention to the fact that, from a taxonomic perspective, the incidence of cases was strikingly patchy (Kirkwood, J.K. & Cunningham, A.A. (1994) Epidemiological observations on spongiform encephalopathies in captive wild animals in the British Isles. Veterinary Record 135, 296-303: J/VR/135/296). Also Kirkwood, J.K., Cunningham, A.A., Flach, E.J., Thornton, S.M. & Wells, G.A.H. (1995) Spongiform encephalopathy in another captive cheetah (Acinonyx jubatus): evidence for variation in susceptibility or incubation periods between species? Journal of Zoo and Wildlife Medicine 26, 577-582) Compared with many other species of exotic ruminants, few kudu were present in the UK but there had been 6 cases of SE among them. The picture seemed similar in the felids. Compared with other species of exotic felids (eg lions in which no cases had occurred), there were relatively small numbers of puma and cheetah in the UK but (at that time) there had been 3 and 4 cases among these respectively. Almost certainly a wider range of species were exposed to contaminated feeds than those in which cases have occurred or been detected. However, we were cautious about drawing firm conclusions about variation in susceptibility between species because (i) incubation periods vary between species and we thought other cases may emerge and (ii) because the variation might be related to differences in intensity of exposure.
16. The number of cases of SE each year in zoo hoofed-stock reached a peak around 1991 and has declined since as shown in the figure below (this and the subsequent figure are updates of those I showed at the Royal College of Pathologist’s Meeting on TSEs at the Royal Society on 4th July 1996). This pattern suggests that the ban on including RDP in ruminant feeds has been an important factor in the control of the disease in zoo bovids.
17. The number of cases in zoo felids, since the first case was diagnosed in 1991, has averaged 2 per annum. The difference in this pattern between the felids and the bovids may be due, at least in part, to the apparently longer incubation periods in felids (inferred from ages at death).

18. In 1993, my colleague Andrew Cunningham (Veterinary Pathologist, IoZ) and I applied for and were awarded a contract with MAFF to undertake a project entitled 'Peripheral tissue distribution of the agent, of spongiform encephalopathy in Greater kudu'. Proposals on this subject were also submitted to the AFRC and to the Wellcome Trust. The former was not successful (it was suggested that the application was more appropriate to MAFF), and the latter was withdrawn following the success of the application to MAFF. The purpose of this project, which started 1st June 1993, was to study of the tissue distribution of infectivity in greater kudu (based on samples collected from some of the cases listed above), since we considered that this study might provide information about possible routes of transmission between animals. Preliminary results suggested that infectivity might be present in tissues other than just CNS but the data were inconclusive. At the request of MAFF, Andrew Cunningham has applied for funds
to continue this work. Another part of the contract was to maintain the kudu group at London Zoo, to allow for monitoring for further cases and the potential for further investigations should further cases occur. Since the end of 1992 there have been no further cases of SE in these animals. It has been impossible, to date, to draw any firm conclusions about the routes of infection in the cases that occurred. Since it was considered from all the evidence available, to be very unlikely that the feed offered to the animals from 1988 onwards could contain RDP, the pattern of incidence in the group between 1989 and 1992 suggested that transmission between animals might have occurred. However, in 1995, it became clear from further discussions with the manufacturers that the possibility that the pelleted feed could have contained RDP for some years after the July 1988 ban, could not be entirely ruled out. MAFF was kept abreast of developments during this project by a series of meetings with the MAFF Project Officer, Mr Ray Bradley. Andrew Cunningham, the Project Leader, submitted a final report to MAFF on 21st February 1997. A further approach was made to MAFF in August 1996 seeking further support for the maintenance of the kudu group. This was not successful. An application was also made to MAFF in December 1994 for funding for a project to investigate if the SE of cheetahs was transmissible to mice and, if so, whether the infectious agent was related to that of BSE. This was unsuccessful as were applications made to the Wellcome Trust and the Whitley Animal Protection Trust on the same subject.

19. As regards dealings with committees, working parties and government departments: the cases in the ZSL animals (and, as far as I am aware, all the zoo animal cases that occurred in the British Isles) were diagnosed or confirmed at the Central Veterinary Laboratory (CVL), and we discussed these with colleagues at the CVL and published a series of papers with them addressing epidemiology and control. The CVL staff were very helpful in sharing their knowledge of spongiform encephalopathies with us. During the period I also wrote to the Spongiform Encephalopathy Advisory Committee describing findings and the pattern of cases in kudu (and other zoo animals) seeking guidance on our approach to controlling SEs in zoo animals and any possible public health risks. The Committee was satisfied with our approach, but noted the apparent marked susceptibility of the kudu and encouraged work on basic biology which might shed light on this (our MAFF-funded project was in line with this and tissues were made available to other scientists on request). As indicated above, I was invited to present a review of cases in zoo animals at the Consultation on BSE with the Scientific Veterinary Committee of the Commission of the European Communities held in Brussels, 14-15th September 1993 (Kirkwood, J.K. & Cunningham, A.A. (1993) Spongiform encephalopathy in captive wild animals in Britain: epidemiological observations. In R. Bradley & B Marchant (Eds) Transmissible spongiform encephalopathies. Proceedings of a Consultation on BSE with the Scientific Veterinary Committee of the Commission of the European Communities, 14-15 September 1993, Brussels. European Commission. Pp 29-47). (M9 tab 46)
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