REPORT OF A VISIT TO MARWELL ZOO 21.7.86.

Those present: R G Holmes; P Bircher; M Jeffrey

Purpose of Visit

To investigate spongiform encephalopathy in a nyala (Tragelaphus angasi).

Background

Clinical nervous disease was diagnosed in a nyala (F22) at Marwell Zoo. Subsequent neuropathological examination showed spongiform changes of the neuropil and characteristic neuronal vacuolation such as are found in the spongiform encephalopathies chronic wasting disease of Mule deer (Odocoileus hemionus hemionus) and Elk (Cervus elaphus nelsoni); Scrapie of sheep and goats; transmissible mink encephalopathy and kuru and Creutzfeldt-Jakob disease of man.

Marwell Zoo occupies a 100 acre site in Hampshire and contains one of the best collections of African antelope in Britain. Several breeding groups of rare and some endangered bovidae have been established and included in this group is the nyala. (Tragelaphus angasi).

Most of the nyala are kept on hard-standing and have no contact with other deer or antelope but two males (including M19, a sibling of F22) are kept in a grass paddock and these have fence-line contact with oryx (oryx dammah).

The group consists of 18 individuals, 10 females and 8 males. Most of the males are sub-adult and are currently run with the females. The dam of F22 is F19, and was born on 21.4.80 at Marwell. M9, the sire of

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F22, was also born at Marwell on 6.8.78. Two siblings of F22, both sired by M9 are sub-adult males aged about 3 years and 6 months (see fig 1.). None of these animals shows clinical signs of nervous disease.

Anamnesis of F22

Initial clinical signs consisted of a mild hind limb ataxia. Subsequently brief episodic neck twisting (torticollis) and head-tilting with occasional opisthotonic spasms were also seen. Pruritis of the rump and constant licking of the tail-base led to excoriation and ulceration of skin in the tail region. Increased frequency of micturition was also present. Treatment consisted of antibiotic (terramycin), cortisone (dexamethasone) and anthelmintic (ivermectin) therapy, to no effect. The animal progressively deteriorated and F22 was killed 3 weeks after the onset of clinical signs.

The nyala have no known contact with other ruminants apart from the previously mentioned fenceline contact with oryx all of which are healthy. A small number of sheep (2 Suffolks) are kept in the childrens zoo but these animals have no contact with the nyala. F22 was, however, hand reared by a keeper who also had responsibility for a small number of sheep.

No American deer have been imported into the zoo and none of the African antelope are known to have had contact with American deer from Colorado or Wyoming.

Mink are not kept at the zoo. Questioning of staff at Marwell suggests that there has been no incidence of chronic nervous diseases in human in contacts.

Discussion

The clinical and neuropathological findings in F22 are consistent with the spongiform encephalopathies of animals and man. The agents causing spongiform encephalopathy in various species cannot be unequivocally distinguished and some isolates of human agent cause neurologic disease in goats indistinguishable from scrapie. The spongiform encephalopathies are invariably fatal once clinical signs of disease are evident and as very high fatality rates (79% of 67 animals) are recorded in Mule deer it is important that an awareness of the disease is maintained at Marwell.

Much is still to be learned about these encephalopathies particularly in deer and control strategies for antelope at Marwell can only be based on information obtained from observations in other species, noteably in Mule deer, sheep and the experimental model of scrapie in mice. Some important observations of the biology, transmission and control of scrapie on which a disease control strategy might be based is therefore summarised below.

Biology of Scrapie

Scrapie is caused by an undefined infectious agent which exhibits strain variations. Genetic variations in the agent interacts in vivo with genetic variation in the host to produce many possible outcomes of infection in terms of incubation period and brain pathology. Most naturally occurring cases in sheep and goats occur between 2½-5 years and duration of clinical signs ranges from 2 weeks to 6 months. The natural history and clinical course of the disease varies with breed. (Mule deer show a similar age of onset and duration of clinical signs but signs are very different from those seen in sheep).

In mice and sheep experimentally inoculated with scrapie the agent initially replicates in extra-neural tissues, principally in lymphoreticular tissue and in the intestine suggesting that natural infection is acquired by the oral route. In mice the agent passes via visceral nerves to the CNS and is first present in the CNS at the thoracic spinal cord. It spreads rostrally, apparently along neurites, to infect sequentially the cervical spinal cord, brainstem and finally the cerebrum. Depending on the virus strain and the genotype of the host the period between inoculation and development of clinical disease is variable and may be exceedingly long. In some instances the disease may remain sub-clinical throughout a natural life span.

There is a strong familial occurrence of the disease. Although the epidemiological importance of the close association of an infected ewe with her lamb (vertical transmission) is well documented the mode of transmission of infection from dam to progeny is still uncertain but the placenta is known to be highly infected with the agent. Horizontal transmission is also known to occur but scrapie under natural conditions is not highly contagious. The infectious agent has not yet been demonstrated in the urine, saliva or faeces of naturally infected sheep and goats.

Diagnosis

There are currently no serological methods available for the detection of an immune response to infection in-vivo and there are no in-vitro methods of detecting the infectious agent. The disease can therefore be diagnosed only as a clinicopathological entity. That is, it is a recognisable combination of clinical signs accompanying characteristics, though not specific, changes in the brain. In some

breeds of sheep, noteably the cheviot breed, infected with some strains of the agent the clinical picture may not be as stereotyped as in other breeds and the lesions in the brain may not be as easily demonstrable as often described. In one study 13% of clinically overt cases did not show clear diagnostic lesions. Nevertheless a diagnosis of scrapie in most sheep can usually be made with confidence based on the clinical history, and histological changes in the brain.

The relationship between onset of clinical signs, and the development of histological lesions in the brain has not been established in sheep but in mice it is well established and experimental evidence suggests that in some regions of the brain spongy changes are present before the clinical stage of scrapie.

Control

Currently the only effective means of controlling the disease in sheep flocks is by rigorous culling or by increasing resistance by genetic manipulation.

Experimental infection of a wide range of sheep breeds has shown that some breeds are resistant to disease. For example scrapie has not been found in Soay or Dorset horn breeds. Moreover selection within breeds may permit the development of at least two different phenotypes permitting selection for resistant and susceptible flocks. For three breeds of sheep, Cheviot, Herdwick and Swaledale, a dominant allele controls susceptibility to infection. In the case of Herdwick sheep heterozygotes develop disease later than do animals homozygous for the susceptible gene.

Recommended Control Strategy for spongiform encephalopathy in nyala at Marwell

1. There are insufficient numbers of nyala to permit the introduction of a culling policy. The situation might quickly arise where too few animals remain to maintain a viable breeding unit. The only other option that remains is to institute a recording system that will permit the selection of animals genetically resistant to disease. Animal F19 is probably infected, if comparisons with chronic wasting disease of Mule deer and with scrapie of sheep are valid. Mule deer develop clinical disease between 2½-4 years of age. At 6 years old F19 is outwith this range and it is therefore possible that she is resistant to disease and breeding from F19 by another male is recommended. Comparisons with scrapie infected sheep might also suggest that both siblings of F22 are likely to develop disease and should therefore be closely observed. If not already available data recorded for each animal should include the following

i) Date of entry to zoo

ii) Origin and intermediary contacts

iii) Date of birth

iv) Sex

v) Dam (identification)

vi) Sire (identification)

vii) Single or multiple birth and identification of sibling(s)

viii) Date on onset and detailed description of any clinical signs.

ix) Fate (ie circumstances of death)

x) Date of death/euthanasia

2. As placentae may be a potent source of infective material, if feasible parturient females should be placed into isolation accommodation reserved for this purpose and the afterbirth obtained and incinerated.

3. Although scrapie is not considered highly contagious it would nevertheless be prudent to eliminate contact with other antelope and deer as far as is possible. (Consideration should be given to putting a double fence between the oryx and the grass paddock containing the two male nyala.)

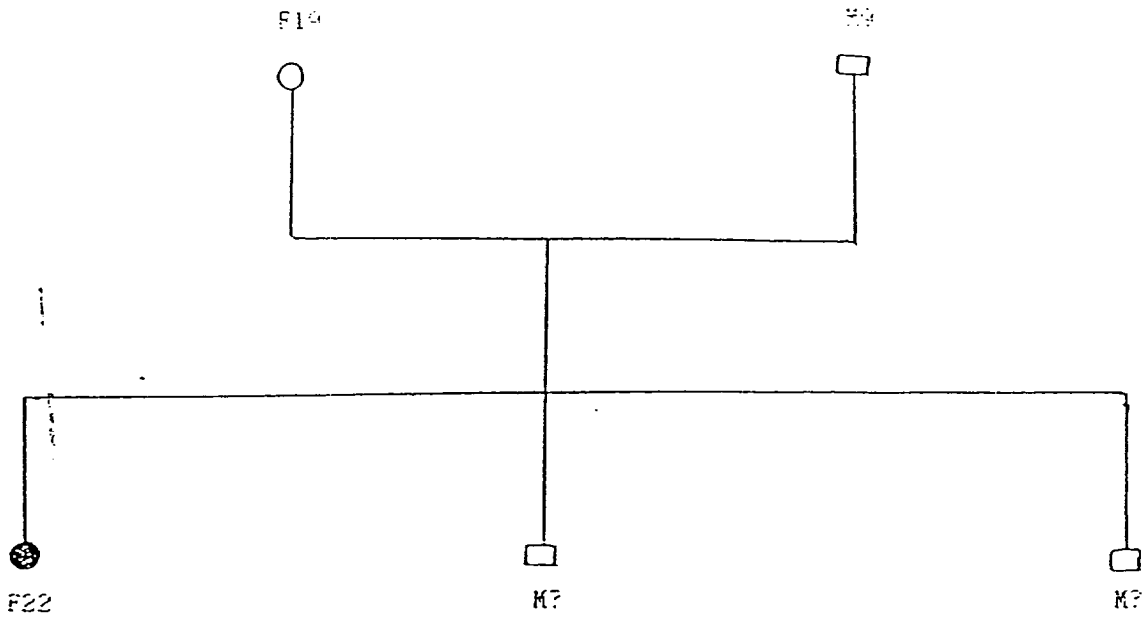
4. Necropsies should be carried out on all antelope which die or have to be killed unless a cause of death or disease is clearly established (eg trauma). In addition brains and preferably also the eyes, from all nyala should be submitted for histopathological examination irrespective of the cause of death.

M Jeffrey

5 August 1986

Figure 1

Pedigree of affected nyaia.



Legend

affected female

unaffected female

unaffected male

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