

BSE/19
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CONFIDENTIAL

Dr Jefferys
Mr Hagger

From: Dr H Pickles

Date: 13 September 1990

Copy: Dr Metters
Dr Richardson
Dr Harper
Mr Murray

SPONGIFORM ENCEPHALOPATHY IN PIGS

We spoke again about the meeting of the Tyrrell committee on the 19 September. The attached paper has been circulated to members as a draft of the sort of advice they might like to give to Ministers, based on the preliminary discussions on the 7 September. We expect MAFF Ministers to want to make the advice public as soon as possible.

Dr Metters feels if the matter of pharmaceuticals/devices is raised in this note, then it should be mentioned as having been referred to the Department of Health, rather than to the MCA and MDD as here. But it would be easier for us if pharmaceuticals/devices are not directly mentioned at all. Subject to your views, I was going to propose to the meeting on the 19th that para 7 of their note is amended to read only:

"7. There are no new implications for human health from the consumption of pig meat in the fact that a pig has shown itself susceptible under laboratory conditions."

H Pickles

Hilary Pickles
Room 414
Eileen House
Ext: 22832

IN CONFIDENCE

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SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE

TRANSMISSION OF BOVINE SPONGIFORM ENCEPHALOPATHY (BSE) TO A PIG

Introduction

1. This paper considers the implications of the experimental transmission of BSE to a pig at the Central Veterinary Laboratory (CVL).

The experiment

2. The work is described in the Annex. We accept the conclusion reached by CVL that it provides incontrovertible evidence of the transmission of BSE to the animal concerned. The following points should be emphasised:

- (i) The animal became affected following artificial inoculation with infected material. This result demonstrates that the species is susceptible to BSE, and thereby provides the first evidence of which we are aware of the susceptibility of pigs to any form of spongiform encephalopathy. But it does not indicate the degree of susceptibility. Nor does it provide any evidence that pigs might be susceptible under natural conditions nor will it show whether there might be any difference between breeds (because of the restricted range of animals used in the experiment).

- (ii) We have seen a video record of the affected pig. We do not believe that the symptoms shown by the animal would have been easily confused with those of another condition. It therefore seems unlikely that the disease has occurred unnoticed in the field. While the vast majority of pigs are slaughtered before clinical symptoms would be expected to manifest themselves, there are a large number of sows and boars in the herd, sufficient for the distinctive symptoms to have been revealed, should these occur. None have been reported. On the evidence of this case, the symptoms are sufficiently distinctive for an effective surveillance programme to be feasible.
- (iii) So far, only one of the eight surviving animals that were subjected to an identical challenge has succumbed to clinical disease. If the rest of the group fails to express disease, this result would be atypical for a spongiform challenge. It could suggest that most pigs are resistant even to the inoculation into the brain of large quantities of diseased material, and that to ensure valid negative results larger groups of test animals would be required for certain species.
- (iv) Many questions remain unanswered. If pigs have not in the past been shown to be affected by a spongiform encephalopathy, does the fact that one has become affected now reflect the inadequacy of previous experiments, the failure of past surveillance, the heavy dose of infection and efficient route for transmission used in the present experiment, or that the

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agent causing BSE is different from that causing scrapie, to which pigs have presumably been exposed for years through their feed? Further experiments would need to be conducted in order to establish

- the susceptibility of pigs by the oral route;
- which tissues in porcine animals were capable of transmitting infection;
- a comparison of the effects of BSE and scrapie on pigs

Future action

3. In addition to the experimental work described in 2 (iv) above, we would stress the importance of continuing surveillance of developments in the field in order to ascertain whether a spongiform encephalopathy has developed in pigs in natural conditions. Systematic and coordinated study of the similar condition that has been noted in cats in recent months is also important, and we note that action has been taken in this area. Epidemiological work based on these data, coupled with any information that emerges about the disease in pigs, could provide pointers as to whether the infection is related to the particular circumstances of the experiment or suggests a change in the scrapie agent.
4. It is very difficult to draw conclusions from one experimental result for what may happen in the field. We also recognise that the proportion of cattle going for slaughter which might have been directly exposed to the BSE agent is now relatively low and falling. But we do not believe in the light of the latest evidence that it makes sense for material that is likely to carry the BSE

agent to be used in feed for susceptible species. This would require that the same specified bovine offals already excluded from human consumption should be excluded from the feed used for such species.

5. Although the relationship between BSE and the finding of a spongiform encephalopathy in cats has yet to be clarified, the fact that this has occurred suggests that a cautious view should be taken of those species which might be susceptible. We therefore believe that the "specified offals" of bovines should be excluded from the feed of all species. We are aware that many feed compounders and pet food manufacturers are already applying such an exclusion in practice.
6. We see no grounds for extending to feed for non-ruminant species the ban on the feeding of ruminant protein to ruminants that was introduced in July 1988. Pigs, and other species, will in particular have been exposed for many years to material from scrapie-infected sheep without apparently developing a spongiform encephalopathy.
7. There are no new implications for human health in the fact that a pig has shown itself susceptible under laboratory conditions. If there is a hypothetical risk, it is highest where porcine material is used in preparations which are injected or implanted into human beings. We believe that this should be brought to the attention of the Medicines Control Agency and the Medical Devices Directorate.
8. If clear evidence were to emerge that a spongiform encephalopathy occurs in British pigs in field conditions, this would raise new issues which would require further examination.

PARENTERAL TRANSMISSION OF BSE TO THE PIG

This is an interim report prepared at the request of the Spongiform Encephalopathy Advisory Committee, on the experimental paranteral transmission of BSE to the pig.

The report outlines the experimental design of the study and the clinical and pathological findings in a single challenged pig (PD115).

Experimental design:

Inoculum A ten per cent saline suspension of pooled brain stem homogenate was prepared from four natural cases of BSE (the same animals as those used in the initial mouse, hamster and cattle transmission studies). Saline served as the control inoculum.

Experimental Animals: Ten 1-2 week old piglets were each inoculated under halothane anaesthesia with brain suspension:

- 0.5ml intracranially (i/c) by percutaneous transcalvareal injection into the left cerebrum
- 1-2ml intravenously (i/v) into the left jugular vein
- 809ml into the peritoneal cavity (i/p)
- (PD115 received 0.5 ml i/c, 1.0ml i/v and 8.5ml i/p)

Eleven control piglets were inoculated similarly with saline. All inoculations were made in late February and early March 1989. Challenged and control pigs were housed separately in loose boxes in groups of 2-3. Clinical observation was undertaken 3-4 times weekly.

Clinical Observations:

The first clinical signs in pig PD115 were observed approximately 481 days post inoculation. They included mild aggression (to handlers), intermittent inappetence and depression. Within one week of the onset inexplicable random biting activity, swaying whilst standing, mild pelvic swaying whilst walking and inappetence were apparent. The pelvic limb ataxia persisted and was later accompanied by aggression, periods of apprehension of familiar and unfamiliar objects and uncharacteristic reluctance to leave the pen. Defecation was no longer confined to the normal dunging area.

One week before termination PD115 showed progressive generalised weakness and increasingly required assistance to stand. Occasionally spontaneous falling occurred. Aggression was not apparent at this stage but there was constant following and nuzzling of the handler.

At termination (31 July 1990), five weeks (35 days) from onset of clinical signs, the pig had behavioural changes, ataxia, weakness and loss of bodily condition. When examined on 31 July it showed frequent rooting behaviour in straw bedding and restless pacing. Repeated attempts to lie down were made and then seemingly abandoned, the standing posture was constantly shifting and there was generalised limb weakness. There was a generalised gait ataxia with hypermetria. The stance was widebased. The ears were symmetrically abnormally positioned, dropping whilst the pig was standing, giving a "depressed" facial expression, or directed back in a "fixed" position when the pig was recumbent. General bodily condition was fair with a markedly reduced body weight and a "hairy" coat compared to the control littermates.

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Macroscopic Observations:

There was no gross major organ pathology.

There were no significant gross observations of fixed brain material.

Microscopic observations:

Brain:

- Spongiosis of grey matter throughout major brain areas with greatest intensity in medial geniculate body, superior colliculus and corpus striatum.
- Vacuolation of perikarya sparsely represented in dorsal nucleus of the vagus nerve.
- Widespread astrocytic response.

Diagnosis:

Spongiform Encephalopathy

Conclusions:

The changes in PD115 are unequivocally those of a scrapie-like encephalopathy. The clinical history of this animal also provides strong supportive evidence of a scrapie-like disease.

The result, albeit confined to one animal in the experimental challenge group is incontrovertible evidence of the transmissibility of BSE to the pig by simultaneous intracerebral, intravenous and intraperitoneal inoculation with an incubation period of approximately 481 days.

This indicates the previously unrecognised susceptibility of the pig to a scrapie-like disease and extends the experimental host range of BSE. Like the results obtained from similar studies in mice and cattle the finding provides no information on the probability of disease occurring in pigs from natural dietary exposure.