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BSE : TIME TO TAKE H.B. PARRY SERIOUSLY

Sir,

No doubt you will all have heard of BSE (it is after all to be a notifiable disease), but have you heard of H.B. Parry? You will find that the Sixth edition of Veterinary Medicine by Blood, Radostits and Henderson (Bailliere Tindall, London) is dedicated to him; but why?

Parry believed that scrapie was a hereditary condition of sheep, passed on in an autosomal recessive fashion. Parry was regarded as a heretic - after all, any fool knows that scrapie is an infectious condition of sheep, don't they? How can a genetic condition possibly be transmissible? I shall attempt to explain.

PrP<sub>33-35</sub><sup>C</sup> is a normal cellular protein produced in all mammalian cells thus far studied. In scrapie and related conditions, this protein is altered such that it becomes protease resistant (PrP<sub>33-35</sub><sup>SC</sup>). PrP<sub>33-35</sub><sup>SC</sup> occurs only in the transmissible spongiform encephalopathies, and forms a major component of scrapie associated fibrils (SAF). The findings of SAF (Wells et al, 1987) and PrP<sub>33-35</sub><sup>SC</sup> (Hope et al, pers.comm.) in BSE brain tissue leave no doubt that BSE is caused by a scrapie-type agent [BSE also shares common histopathological changes with the other transmissible spongiform encephalopathies, such as grey matter vacuolation (Wells et al, 1987) and astrocytic hypertrophy (McGill & Wells, paper in preparation)]. As yet, scrapie infectivity has never been separated from PrP (see Prusiner, 1987) and in my opinion the most likely form of the agent is a shell of host protein (PrP<sub>33-35</sub><sup>SC</sup>) surrounding and protecting a small amount of nucleic acid (a "virino" - see Hope & Kimberlin, 1987).

The term "genetic susceptibility to scrapie infection" is constantly used by many authors. Such "genetic susceptibility" has never been proven. All that has been proven is that incubation times for scrapie agents are affected by host genotype. With the exception of kuru (probably spread by cannibalism) and Gerstmann-Straussler syndrome (GSS - see later) of humans, all the established transmissible spongiform encephalopathies have had scrapie of sheep implicated in their origins [Creutzfeldt-Jakob disease (CJD) of man, transmissible mink encephalopathy (TME) of farmed mink, chronic wasting disease (CWD) of mule-deer and scrapie of goats]. Why are sheep such a nidus of infection?

Two conditions which result in a spongiform encephalopathy and are hereditary have recently been shown to be transmissible. The first is the grey tremor mutant mouse (not caused by a scrapie type agent) (Hoffman et al, 1987) and the second is GSS (which is caused by a scrapie-type agent)

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(Baker et al, 1985). Scientific opinion again employs the unproven "genetic susceptibility to a widespread agent" theory to explain these phenomena. There is no logic in this approach. Is it not far more likely that the above two conditions are caused by the derepression of a cellular "virogene"? I have already mentioned that part of the agent may well be formed from a host protein (PrP<sub>33-35</sub><sup>SC</sup>) - why should not the whole agent be made from host components?

In simple terms, what I am suggesting is that the scrapie agent is generated de novo from ovine DNA, and thus scrapie is a hereditary and transmissible disease.

This is a line of thought which must not be allowed to die with H.B. Parry.

To fully explain why I believe such heresy would take up a whole issue of Veterinary Record, and hence I have not fully elaborated or given a reference for each point I have made. The following reference list is adequate as an introduction to the subject.

If the scrapie agent is generated from ovine DNA and thence causes disease in other species, then perhaps, bearing in mind the possible role of scrapie in CJD of humans (Daviniour et al, 1985), scrapie and not BSE should be the notifiable disease.

Yours faithfully,

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