
COMMENTARY

Eradicating scrapie

J. HOPE*

Veterinary Laboratory Agency, New Haw, Addlestone, Surrey, UK

(Accepted 17 February 2009; first published online 9 April 2009)

Sheep farmers have coped with scrapie for centuries and several rules of thumb were formed into disease management practice after the Second World War when transmission of the disease was believed to be caused by a filterable, ‘slow’ virus. These management rules were influenced by experience and the notion of a scrapie virus; they included the culling of the maternal line of an affected sheep, avoiding contact between lambing ewes, burning placentae and foetal membranes after birth, and disinfecting building and lambing pens known to contain affected animals by dousing with solutions of washing soda. These methods of animal husbandry remain useful today although we now believe the disease is the product of a rogue protein – the prion protein (PrP^C) – and represents a unique type of transmissible protein-folding disorder.

The emergence of the prion-protein-agent hypothesis in the early 1980s changed our thinking about scrapie. This conceptual change was accelerated by an epidemic of this type of disease which occurred in cattle (bovine spongiform encephalopathy; BSE) from the mid-1980s and, in 1996, the correlation of the incidence of BSE to a human form of fatal, neurological disorder, variant Creutzfeldt–Jakob disease (vCJD). Epidemiological modelling has been a key tool in controlling the BSE epidemic and an extended common point source for the epidemic was identified at an early stage: the incorporation of meat and bone meal (MBM) in cattle feed rations. Elimination of this source of infection curtailed the worst effects of the

BSE epidemic and the annual incidence rate in the UK has fallen to <8 cases per million adult cattle in 2008 from a peak incidence of over 30 000 cases per year in 1992. For the past decade, extensive surveillance of cattle and human cases for BSE and vCJD, respectively, support a link between the two diseases but has failed to confirm where the infectivity in MBM originated.

Experimental transmission of BSE to sheep or goats produces a prion-protein-related, fatal, neurological disease similar in its clinical signs to scrapie although this disease has molecular and immunohistological characteristics which differ from those of the natural disease. Only one (or possibly two) cases of a prion-protein-related disease with the characteristics of experimental BSE in small ruminants have been found naturally in goats and none in sheep. However, fears that BSE might propagate in sheep and goats masked by scrapie, and that their carcasses or secretions could act as a secondary source of human exposure to BSE, have stimulated a European Union (EU) initiative to eradicate prion diseases (also known as transmissible spongiform encephalopathies; TSEs) from small ruminants. In 2001, the European Union Scientific Standing Committee (EU SSC) on TSEs were unanimous in stating that screening out infected animals by testing was impractical because of the lack of a suitable ante-mortem test and that the widespread dissemination of TSE infectivity in small ruminants made a simple policy of removal of ‘risk’ materials from the carcass inadequate to protect the consumer from foodborne exposure. The EU SSC compiled a rigorous risk assessment and management plan for the control of TSEs in sheep and, as a key element of that plan, recommended selective breeding of sheep for alleles of the prion protein gene known to

* Author for correspondence: Dr J. Hope, Lasswade Veterinary Laboratory, Pentlands Science Park, Bush Loan, Penicuik, Midlothian EH26 0PZ, UK.
(Email: j.hope@vla.defra.gsi.gov.uk)

confer relative resistance of animals to clinical disease.†

In the UK, following a recommendation from the Spongiform Encephalopathy Advisory Committee (SEAC) (Defra's independent think-tank for TSE/prion issues), Defra took the initiative and, in July 2001, inaugurated the National Scrapie Plan (NSP) with the aim of reducing the frequency of the prion protein allele most frequently associated with classical scrapie – the VRQ allele‡. Other EU countries adopted different strategies, notably The Netherlands where there was aggressive selection of animals carrying the allele (the ARR allele of the ovine prion protein gene) that appears to confer most resistance to classical scrapie and experimental BSE. The PrP genotyping of sheep in Great Britain has since continued as part of the Ram Genotyping Scheme (RGS), and the more recent Voluntary and Compulsory Scrapie Flocks Schemes (CSFS) which include movement controls and active culling of carriers of higher risk alleles in confirmed scrapie-infected flocks (the CSFS requires culling of all ewes other than ARR/ARR and ARR/X, where X is not VRQ). Due, at least in part, to these interventions, there has been a significant drop in the number of scrapie cases confirmed in clinical suspects referred to the veterinary authorities between 2002 and 2007 and a reduction in the incidence of disease detected by active surveillance of healthy cull ewes at the abattoir and in sheep found dead on-farm. But how long do we need to continue with these schemes in order to eradicate scrapie?

In this issue, two papers by Truscott and Ferguson [4, 5] use various data obtained by passive and active surveillance of sheep, and by genotype profiling of different breeds in the national flock, to model the impact of the various parts of the NSP on the number of confirmed cases, the frequency of PrP alleles and the basic reproduction ratio (R_0) for classical scrapie within the framework of a large simulation model of the British sheep population and its breeding and trading structure. Their baseline scenario was one of non-intervention and their model predicts this will lead to persistence of scrapie within the national flock for the next 300–400 years. More optimistically, they

forecast the complete eradication of scrapie within 32 years (95% CI 23–43) as a result of the RGS and that in combination with the CSFS, the RGS will lead to elimination of this disease much faster (some 10 years earlier than with the RGS alone). That may not happen: in December 2006, the SEAC concluded the risk of BSE infecting the national flock, and hence the impact of the RGS on lowering the exposure risk of humans to BSE, was by then negligible and the dismantling of this scheme has already begun. Currently, the CSFS remains and its effective application will be the key to accelerating the eradication of classical scrapie in the future.

ACKNOWLEDGEMENTS

This paper represents the author's personal view and does not necessarily represent the view of VLA or Defra.

DECLARATION OF INTEREST

None.

REFERENCES

1. **Opinion of the Scientific Panel on Biological Hazards.** The breeding programme for TSE resistance in sheep. *EFSA Journal* 2006; **382**: 1–46.
2. **Opinion of the Scientific Panel on Biological Hazards.** A TSE risk assessment from carcasses of ovine and caprine animals below 6 months of age from TSE infected flocks intended for human consumption. *EFSA Journal* 2008; **719**: 1–27.
3. **Bellworthy SJ, et al.** Oral transmission of BSE to VRQ/VRQ sheep in an experimental flock [Letter]. *Veterinary Record* 2008; **162**: 130–131.
4. **Truscott JE, Ferguson NM.** Control of scrapie in the UK sheep population. *Epidemiology and Infection*. Published online: 8 August 2008. doi:10.1017/S0950268808001064
5. **Truscott JE, Ferguson NM.** Transmission dynamics and mechanisms of endemicity of scrapie in the UK sheep population. *Epidemiology and Infection*. Published online: 8 August 2008. doi:10.1017/S0950268808001052.

† These recommendations have recently been re-endorsed in several opinions by the European Food Safety Authority [1, 2] even though it has emerged that these 'resistant' animals may still be susceptible to another form of prion-protein disease, Nor98 or atypical scrapie.

‡ Paradoxically, experimental BSE develops much more slowly in VRQ/VRQ sheep than in some of the genotypes favoured by this selection policy [3].