Bovine spongiform encephalopathy in Great Britain: A case-control study of cases born after 31 July 1996

Wilesmith, J.W.[1], Stevenson, M.A.[2], Morris, R.S.[2], Benard, H.[2], Arnold, M.[3], Ryan, J.B.M.[3], Burke, P.[1]
[1]Animal Health and Welfare Directorate General, 1A Page Street London SW1P 1PQ, England; [2]EpiCentre, IVABS, Massey University, Palmerston North, New Zealand; [3]Epidemiology Department CERA Veterinary Laboratories Agency (Weybridge), New Haw, Addlestone, Surrey, KT15 3NB, England

Abstract

Epidemiological studies of cases of BSE in animals born after the initial feed ban in Great Britain in July 1988 provided conclusive evidence that cross-contamination, notably within feed mills, of cattle feedstuffs was a reason for continued exposure. As a result, a total ban on the feeding of mammalian derived protein to all farm animals was introduced on 1 August 1996. The first case of BSE in an animal born after this re-inforced ban (BARB case) was reported on 8 May 2000. The continued collection of epidemiological data has allowed a range of epidemiological analyses of this and the subsequent BARB cases that have been identified. These have shown that the risk of infection for animals born after 31 July 1996 was dramatically reduced by this ultimate ban. The geographical risk of infection also changed markedly for the BARB birth cohorts indicating that these cases presented as the third distinct phase of the BSE epidemic in Great Britain. The geographical distribution together with the within herd clustering have been of particular importance in the formulation of hypotheses related to the continued occurrence of cases, albeit at a very much reduced incidence and with evidence of a declining risk in successive birth cohorts. The epidemiological analyses provide evidence for a continued feedborne source.

Introduction

The descriptive epidemiology of the first 93 cases of BSE in cattle born after the introduction of this reinforced feed ban (termed 'BARB' cases in the remainder of this paper) has been presented recently (Wilesmith et al., 2005). The results of those analyses suggested that a continued feed borne source was responsible for at least the majority of cases, and that this was unrelated to the previous indigenous source. This paper describes the results of a case-control study of these cases of BSE to elucidate further their aetiology.

Materials and methods

A case-control study was undertaken to identify risk factors for BSE in cattle born after the 31 July 1996 ban on feeding mammalian derived meat and bone meal to all farmed livestock, horses and fish (HMSO 1996). The target population was all cattle born in England, Wales and Scotland after 31 July 1996. The eligible population comprised those members of the target population born between 31 July 1996 and 15 February 2005 who had either died or were slaughtered by 15 February 2005 and were tested for BSE. The group studied comprised members of the eligible population found to be positive for BSE (cases, $n = 93$) and suspect clinical cases detected on their natal herd which were reported to Defra and for which the confirmatory diagnostic methods for BSE were reported as negative by 15 March 2005 (controls, $n = 376$).

A standard epidemiological questionnaire was completed for all clinical suspect cases which were statutorily reported and slaughtered as BSE suspects and for cases detected by active surveillance. This provided the date of birth of the animal, the enterprise type of each herd, the maximum herd size during the 10-year period before each subject's date of birth, details of management of the case throughout its lifetime, and the easting and northing coordinates of the herd's main farm building. Questionnaire data were used to determine the most likely herd of exposure for purchased cases and the location of the exposure herd, assuming exposure to infection occurred in the first six months of life (Wilesmith, Ryan, and Hueston, 1992). Date of onset of clinical signs was recorded for cases and date of death or slaughter for active surveillance cases which did not have an onset of clinical signs date.

We developed a mixed-effects logistic regression model of factors associated with BARB risk, including a multivariate normal random effect term to account for the clustering of individual study subjects within herds. A penalised quasi-likelihood approach was used, implemented in the `MASS` package (Venables and Ripley, 2002) within R version 2.01 (R Development Core Team, 2004). Herd-level residuals were plotted as a binned omnidirectional variogram to quantify the residual, spatially correlated BARB risk at scales of distance that were small (0 – 50 km) relative to the entire study area. To characterise spatial autocorrelation in residual BARB risk at spatial scales greater than 50 km we plotted the herd level residuals as a kernel density surface. This surface showed the distribution of herds with positive and negative-sign residuals throughout Great Britain: areas with a predominance of positive-sign residuals indicating locations where the number of BARB cases was not explained by the modelled individual subject-level and herd-level explanatory variables and areas with a predominance of negative-sign residuals indicative of locations where BARB case numbers were less than that predicted by the model.

Results

Ninety-three cases and 376 control animals provided data for analysis. Twenty-seven of the 93 cases (29%) were detected as clinical suspects and 66 (71%) by active surveillance. A map of Great Britain showing the location of the case and control herds is shown in Figure 1. Regression coefficients and adjusted odds ratios for the mixed-effects model of BARB risk are shown in Table 1. Figure 2 is a density plot showing the spatial variation in the herd-level residuals from the mixed-effects model shown in Table 1.

Discussion

The protracted incubation period of BSE, with a mean of around 60 months, means that the effects of past control measures can only be assessed belatedly. In the case of the BARB cases, whose incidence is low, meaningful analytical epidemiological studies were only possible after the accumulation of a sufficient number of cases. This prolongs the inevitable delay in the provision of further advice to prevent additional cases occurring in animals born after the ultimate mandatory feed ban controls.

We found no evidence of an association between BARB status and feed type, the presence of other animal species on farm, or exposure to waste products. The last two of these variables were used as proxies for environmental contamination of farms, both directly and indirectly. The results reported here are consistent with the available information on the excretion of the BSE agent from infected cattle.

Our analyses show that herd-level factors accounted for 99% of the total variation in BARB risk, a finding that was expected given that the 469 study subjects were from 435 herds. BARB risk was positively associated with age and negatively associated with the number of pre-BARB BSE cases diagnosed within the herd. Where more than 10 pre-BARB BSE cases had been diagnosed in a herd the probability of a study subject being BARB-positive was less than 0.20. These results are consistent with herd managers applying effective BSE control measures within a herd once the presence of disease had been confirmed. Re-emphasis of specific details of on-farm measures to reduce the likelihood of exposure to infective agent – targeted at herds that have not, to date, experienced a case of BSE – might further assist in reducing exposure to infective agent, and reduce the likelihood of further cases.

After controlling for study subject age and the number of pre-BARB BSE diagnoses we found no evidence of second-order spatial autocorrelation in residual herd-level BARB risk at distances of 0 to 50 km. Kernel density plots of the herd-level residuals from mixed-effects model allowed the first-order pattern of unaccounted-for herd-level BARB risk to be visualised. The observed probability of a herd being BARB-positive was greater than that predicted by the mixed-effects model in the counties of Dyfed, Gwynedd, Avon, Wiltshire, and Oxfordshire (Figure 2). Confluent areas where the observed risk of BSE was greater than that predicted by a model accounting for individual study subject and herd-level effects implies exposure to an off-farm source of infectious agent – for example, intermittent cross contamination of cattle feed by one or more feed compounders that supplied herds in these areas. Re-emphasis of the detail of BSE control measures to feed compounders and cattle herd managers, targeting the counties of Dyfed, Gwynedd, Avon, Wiltshire, and Oxfordshire, should further reduce the likelihood of exposure to infective agent, and further reduce the incidence of BSE in Great Britain.

Table 1 BSE in British cattle born after 31 July 1996. Regression coefficients and standard errors from a mixed-effects logistic regression model of BARB risk.

Variable	Coefficient	SE	t	P	OR (95% CI)
Intercept	-4.2962	0.3081	-13.94	< 0.01	
Previous cases [a]	-0.9513	0.2992	-3.179	< 0.01	0.38 (0.21 – 0.69) [b]
Age at onset (yrs)	1.6776	0.2388	7.026	< 0.01	5.35 (3.35 – 8.55)

Standard deviation of herd-level random effect: 4.6439.

[a] Number of confirmed cases of BSE born before 1 August 1996 on the exposure herd of cases and the natal herd of controls.
[b] Interpretation: for each additional case of BSE born in the herd before 1 August 1996, the odds of being a BARB was 0.38 (95% CI 0.21 – 0.69) times that of controls.

References

HMSO (1996) The Bovine Spongiform Encephalopathy Order. Statutory Instrument 1996, Number 2007, HMSO, London.

R Development Core Team, 2004. R: A Language and Environment For Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0. URL: http://www.R-project.org.

Venables W, Ripley B (2002) Modern Applied Statistics with S. Springer, London.

Wilesmith JW, Ryan JBM, and Hueston W (1992) Bovine spongiform encephalopathy: Case control studies of calf feeding practices and meat and bone meal inclusion in proprietary concentrates, Research in Veterinary Science 52, 325–331.

Wilesmith JW, Stevenson MA, Morris RS, Ryan JBM, Arnold M, and Prince MJ (2005) An epidemiological update of cases of BSE born after 31 July 1996 in Great Britain. A paper prepared for the Spongiform Encephalopathy Advisory Committee (SEAC) and its Special Group on BARBs.

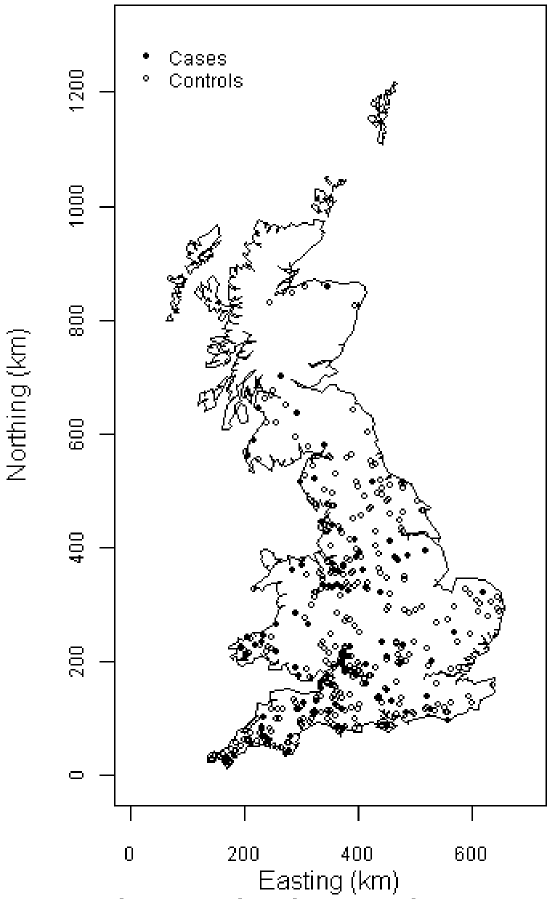

Figure 1 Point map showing case (BARB-positive) and control (BARB-negative) farms described in this study.

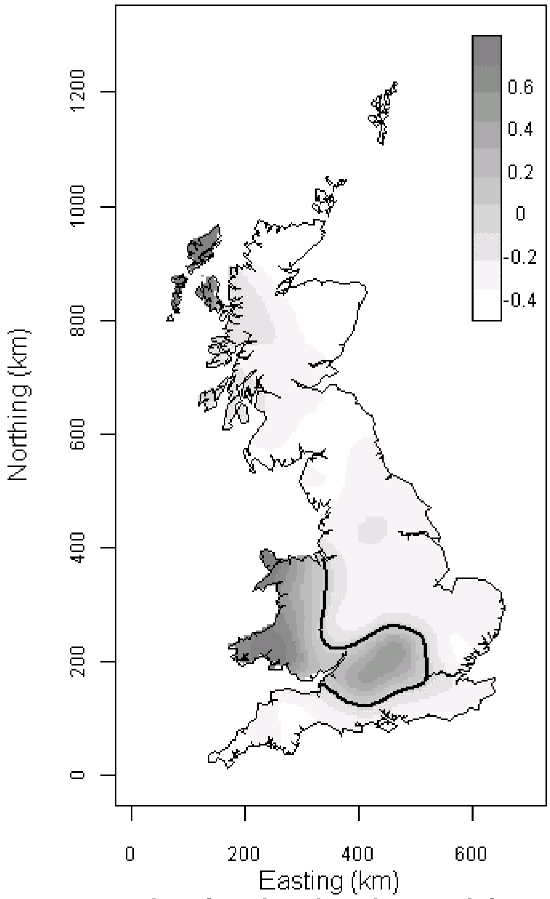

Figure 2 Density plot showing the spatial variation in the herd-level residuals from the mixed-effects model shown in Table 1. The solid contour line delineates areas where the herd-level residuals were greater than zero.