Prediction of future BSE spread

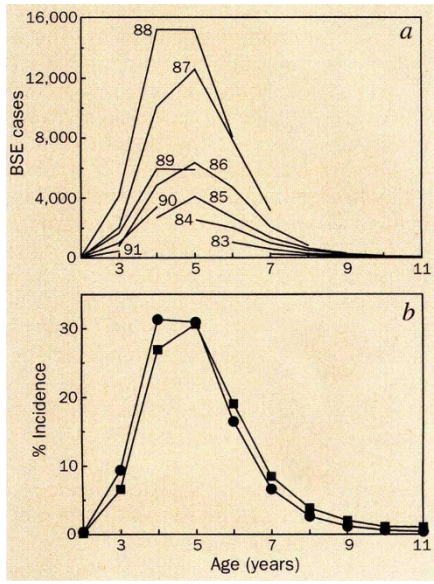
SIR — Spongiform encephalopathies are progressive diseases caused by unconventional infectious agents, now generally believed to be malformed prion proteins[1–3]. At present, there is no test for infection: there is generally a long incubation period between infection and onset of symptoms, and the condition can only be confirmed after death. In 1986 a new form of this disease, bovine spongiform encephalopathy (BSE), was identified in cattle in the United Kingdom[4]. The origin of this disease is believed to be food containing the remains of sheep, and later cattle, that were infected with either scrapie or the BSE agent. In July 1988, the UK government banned the addition of material derived from ruminants to cattle feed. To date, about 160,000 cases of BSE have been reported in the United Kingdom, out of which at least 28,000 occurred in animals born after the food ban; there has been a continued use of contaminated food[5–7]. Many more animals are likely to have been infected but were slaughtered before symptoms developed.

Extensive data are now available on the number of BSE cases in different age cohorts of cattle in the past 5 years[8] (we are most grateful to J. Wilesmith, J. Ryan, L. Hoinville and their colleagues at the Central Veterinary Laboratory for their generous help with data), and we report here results of the simplest of the initial analyses on the dynamics of the disease. Making certain assumptions, we can determine if there have been changes in the age pattern of cases and can predict the number of future cases in different age classes. The figure (*a*) shows the number of BSE cases in different age cohorts (animals born in a given year). The shapes of these curves are very similar, with a peak between 4 and 6 years of age.

The data provide information on $x_i(t)$, the number of BSE cases with a clinical onset in year t in animals aged i years. Here, i goes from 2 to 11 years and t from 1989 to 1994. The figures for 1995 are not yet final, because there are still a few cases being reported with an onset in 1995. Most animals are infected within the first year of life, when the use of feed containing ruminant protein is high[5]. If there is a non-changing, age-dependent frequency of expression of disease, then $x_i(t)$ can be written as $x_i(t) = I(t-i)P_i$, where $I(t-i)$ is the number of animals infected in year $t-i$ and P_i is the probability that an animal infected in its first year of life exhibits the disease at age i. We can then estimate the relative incidence rate, P_{i+1}/P_i, from the quantities $r_i(t+1) = x_{i+1}(t+1)/x_i(t)$, and make predictions for subsequent years. There is, however, a slight trend for $r_i(t)$ to decrease with t, which indicates a small shift of the incubation period to disease expression at a younger age (*b* in the figure).

Therefore, we present two types of predictions. For the first prediction we use the average $\bar{r}_i = \sum_t x_{i+1}(t+1)/\sum_t x_i(t)$ as estimators. For the second model we use $\bar{r}_i = r_i(1994)$ as the most recent estimators. In both cases, we then predict $x_{i+1}(1995) = \bar{r}_i\, x_i(1994)$, and similarly each subsequent year using the prediction for the previous year. Because $r_i(t)$ values are decreasing slowly with time, the second model gives a lower estimate; if this trend reflects a change in the underlying dynamics during the course of the epidemic, the second estimate should be more accurate.

In the table we give, by age cohort, the number of cattle predicted to develop BSE over the next 5 years. A comparison of the predicted number of cases for 1995 with the as yet incomplete data for 1995 gives close agreement: 13,267 confirmed cases, which are likely to constitute at least 90% of the total cases, compared with 13,880–16,110 predicted. From 1996 until 1999, we expect between 15,000 and 24,000 cases of BSE to arise in animals born before 1993. This prediction is representative of the total number only if infection of new animals finally ceases.



a, Numbers of BSE cases in different age cohorts, labelled by year of birth, indicative of common underlying incubation distribution. *b*, Estimates of the age-dependent frequency of disease expression, including background mortality. Squares, the estimate using an average over all the data; circles use only the data from 1993 and 1994. Both estimates give peak incidence of disease at 4 and 5 years of age. There appears to be a slight shift towards expression of the disease in younger cattle in later years.

On the basis of our predictions and the knowledge of the age distribution of adult animals in UK cattle herds, we can calculate that the highest incidence per capita will be in those animals born between 1987 and 1990, with a marked peak in 1988, the year in which the ban on animal supplements in feed was introduced. The lowest per capita and absolute incidence will be in cattle currently aged 10 or more years, as the age-dependent frequency of disease expression is past its peak. About 75% of future cases will occur in animals born in 1989 or later (at least 5 months after the feed ban); this reflects the mid-age peak of the age distribution for the expression of the disease (see figure) and the continuing, though diminishing, rate of infection[5].

PREDICTION OF THE NUMBERS OF BSE CASES BY AGE FOR THE YEARS 1995–99

Age	1995	1996	1997	1998	1999
3	330–490 (435)				
4	1,520–1,860 (1,660)	1,100–2,000			
5	3,360–3,870 (3,221)	1,510–2,120	1,090–2,280		
6	3,120–3,650 (2,942)	1,790–2,410	800–1,320	580–1,420	
7	3,260–3,620 (2,957)	1,260–1,630	720–1,080	320–590	230–640
8	1,260–1,420 (1,021)	1,290–1,620	500–730	290–480	130–260
9	370–440 (311)	570–760	590–860	230–390	130–260
10	150–160 (117)	190–240	290–420	300–480	110–210
11+	90–120 (67)	100–150	130–230	200–390	210–450
Unknown	420–490 (523)	250–340	130–220	60–120	30–60
Total	13,880–16,110 (13,267)	8,050–11,270	4,250–7,130	1,970–3,870	840–1,880

In each column, the lower estimate is based only on the data from 1993 and 1994, and the higher estimate uses an average over all the data. The few cases of unknown age are estimated at 3% of the total number of cases, as has occurred in the years 1989 to 1994. The numbers in parentheses are the 1995 cases reported to date, thought to be at least 90% of the 1995 cases. Using the lower estimate, we predict ~11,000 further cases between 1996 and 1999 in animals born after the feed ban.

On the basis of our predictions and the knowledge of the age distribution of adult animals in UK cattle herds, we can calculate that the highest incidence per capita will be in those animals born between 1987 and 1990, with a marked peak in 1988, the year in which the ban on animal supplements in feed was introduced. The lowest per capita and absolute incidence will be in cattle currently aged 10 or more years, as the age-dependent frequency of disease expression is past its peak. About 75% of future cases will occur in animals born in 1989 or later (at least 5 months after the feed ban); this reflects the mid-age peak of the age distribution for the expression of the disease (see figure) and the continuing, though diminishing, rate of infection[5].

Dov J. Stekel
Martin A. Nowak
T. R. E. Southwood
Department of Zoology,
University of Oxford, Oxford OX1 3PS, UK

1. Prusiner, S. B. *et al.* (eds) *Prion Diseases of Humans and Animals* (Ellis Horwood, Chichester, 1992).
2. Weissmann, C. *Nature* **352,** 679–683 (1991).
3. Prusiner, S. B. *Scient. Am.* **272**(1), 48–57 (1995).
4. Wells, G. A. H. *et al. Vet. Rec.* **121,** 419–420 (1987).
5. Wilesmith, J. W. & Ryan, J. M. B. *Vet. Rec.* **132,** 300–301 (1993).
6. Hoinville, L. J. *et al. Vet. Rec.* **136,** 312–318 (1995).
7. Wilesmith, J. W. *et al. Res. Vet. Sci.* **52,** 325–331 (1992).
8. *MAFF Prog. Reps* (1989–96).