Vet. Res. 34 (2003) 749–760

DOI: 10.1051/vetres:2003032

Original article

Descriptive spatial analysis of BSE in western France

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(Received 19 December 2002; accepted 15 April 2003)

Abstract – The spatial heterogeneity of Bovine Spongiform Encephalopathy (BSE) was analysed on the 84 cases confirmed in western France (WF) between August and December 2000, when both the Mandatory Reporting System and an active surveillance on cattle at risk were running. Ninety-four percent of these cases were born between June 1993 and June 1996, and we analysed the location at birth. One disease mapping and two clustering methods (Scan of Kulldorff and the method of Besag and Newell) were used. In order to attenuate the contrasts artificially created by the standard disease mapping method (over-dispersion), we estimated the Standard Incidence Ratio (SIR) with a Bayesian method (Poisson-Gamma model) allowing a smoothing of the estimators. The geographical location of interest was the "canton", that divided the total area into 526 geographical units. The background population (2.6 million cattle) was obtained from the Agricultural Census 2000. We tested the hypothesis of a homogenous spatial distribution of the BSE risk where the expected number of BSE cases per unit area was obtained by applying the overall BSE rate in WF to each "canton", standardised on the type of breed, dairy versus beef suckler. The SIR ranged from 0.80 to 2.18 and the spatial distribution of BSE cases was significantly heterogeneous. Two spatial clusters were detected with the spatial scan statistics of Kulldorff and the method of Besag and Newell (18 to 20 observed BSE-cases per cluster with a radius of 45 km) centred on the "département" of Côtes-d'Armor and Mayenne. Another cluster was detected with the method of Besag and Newell (9 observed BSE-cases) in the "département" of Finistère. The results proved that the risk of BSE is linked to the geographical location in the area of the study.

disease mapping / Bayesian model / BSE / cattle

1. INTRODUCTION

In France, the first case of Bovine Spongiform Encephalopathy (BSE) was described in 1991 [13]. Since then, the peak incidence of detected BSE cases was reached in 2001 with 273 cases and, all in all, 807 BSE-cases were detected up to March 12, 2003. The main risk factor evidenced for BSE infection is the feeding of animals with meat and bone meal [22]. In France, animal proteins (except dairy proteins as well as poultry, fish and other sea products) have been prohibited from cattle

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feeding since July 1990. Despite this preventive measure, BSE cases appeared on animals born after the feed ban (called BAB cases) [10], and 90% of the BSE cases detected so far in France are BAB cases (URL: http://www.afssa.fr/dossiers/index.asp?id_dossier=1781).

The main hypothesis for the contamination of BAB cases is the cross-contamination between cattle feedstuff and monogastric feedstuff either at the factory, during shipping or on the farm [4, 11, 23]. If this assumption is true, we expect that depending on the context and circumstances, including the importance of the pig and poultry industry and the technology of the feedstuff industry, the BSE contamination risk varies on space. Exploring this assumption requires first to investigate the geographical distribution of BSE cases. Such a spatial analysis of BSE has already been undertaken in Switzerland [8, 9] and in Great Britain [21]. In both countries, BSE incidence has been heterogeneous on a geographical basis and some clusters have been evidenced.

In France the spatial analysis of the BSE epidemic has not been performed so far. The objective of this paper was to explore the geographical risk of BSE in western France (WF), because this region concentrates more than 30 per cent of French cattle, has been historically the most affected with BSE, and has been chosen for a pilot program of active surveillance of BSE using the "rapid" tests [19] and targeted at cattle having died on the farm, subjected to euthanasia or emergency slaughtered after an accident. The data taken into account in our analysis concerned the BSE cases detected between August and December 2000, which corresponded to the pilot study period [18].

We tested different spatial methods relevant to the context (rare event data), one disease mapping and two clustering methods. The disease mapping is a hierarchical Bayesian Poisson-Gamma model. The clustering methods are the spatial scan statistic [14] and the method of Besag and Newell [2].

2. MATERIALS AND METHODS

2.1. Data collection

Epidemiological data on BSE were provided by the "Agence Française de Sécurité Sanitaire des Aliments" (AFSSA Lyon, France), in charge of the monitoring of BSE.

The analysis was restricted to a time period — between 7 July 2000 and 22 December 2000 — and a geographical part of France — WF — to get precise and comparable data on BSE incidence. During this period and in this area, the detection of BSE was based both on the Mandatory Reporting System (MRS), and a targeted surveillance (TS) programme conducted as a census using the Prionics Test® on cattle at risk as a complement to MRS [5]. These two systems were complementary since they allowed the screening of every dead cow.

So, BSE cases taken into account in the analysis were either clinically suspect animals confirmed at the national reference laboratory of AFSSA with Western blot or immunohistochemistry — i.e. cases found with the MRS —, or Prionics® positive animals confirmed with the same two techniques, among the whole cattle population of 24 months old and more, dead on the farm, subjected to euthanasia or emergency slaughtered in the geographical area and period of interest — i.e. cases found with the TS [5, 7, 15, 20].

The geographical location of the BSE cases was the natal holding. The aggregation level of the data was the "canton" (a small French administrative district including five "communes" on the average); WF (Basse Normandie, Pays de la Loire and Bretagne) is divided into 526 "cantons". We did not use a lower geographical scale

because the demographic data on cattle were not available and the number of cases per geographical unit was too small.

It has been evidenced that BSE incidence varies according to the breed (dairy versus suckler cattle) [12, 18]. So, we took this factor into account in the analysis, in particular in the standardisation of BSE cases in mapping the disease.

The background population was assessed by the demographics of the adult bovines having calved. Data were obtained from the Agricultural Census 2000 and are stored on a CD-ROM edited by the Statistics Office of the Ministry of Agriculture and Fisheries (AGRESTE).

The geographical data on the "cantons" perimeters and the "communes" centroids were provided by the GEOFLA® "France Métropolitaine" (IGN© Paris, version 6, 2002).

2.2. Statistical methods

2.2.1. Disease mapping analysis

To elucidate the geographical distribution of disease incidence, and identify the areas with low or high BSE incidence, we used a conventional approach based on the Poisson inference [17]. WF is divided into $n = 526$ "cantons", contiguous areas labelled $i = 1, \ldots, 526$. Let y_i denote the count of observed BSE cases, e_i the number of expected cases and r_i the unknown Standardised Incidence Ratio (SIR) in the area i. It followed from the null hypothesis — the homogenous spatial distribution of the BSE risk — that the expected number of cases e_i was obtained by applying the overall BSE rate in WF to each "canton", standardised on the type of cattle breed, dairy versus beef suckler. The SIR r_i represented an increase/decrease in the risk of contamination compared to a standard risk evaluated on the whole WF area.

We assumed that y_i followed a Poisson-distribution (rare event and large population size). So, the probability of observing y_i cases is

$$f(y_i) = e^{-e_i.r_i}.\frac{(e_i.r_i)^{y_i}}{y_i!}. \quad (1)$$

This basic approach had two limits due to the structure of the data. First, with small geographical units, we observed a high heterogeneity of the at-risk population size because of the small size of the cattle population by geographical unit. This demographic heterogeneity lowered the precision of the estimate of the risk of contamination. Moreover, for a rare disease such as BSE, and with small geographical units, the observed number of cases might often exceed strongly that expected from the Poisson inference. In a given area, the variation in the observed number of cases is due partly to Poisson sampling and also to extra-Poisson variation. Moreover, the Poisson inference does not take into account any spatial pattern. To overcome this problem, Bayesian approaches were used. We considered in the analysis a prior information on the variability of disease rate in the overall area of interest. For this prior information, we assumed that all the true SIR r_i were distributed according to a gamma distribution with mean $\mu = \nu/\alpha$ and variance $\tau^2 = \nu/\alpha^2$, where α is a scale parameter and ν is a shape parameter. The probability function of r_i is then,

$$g(r_i|\alpha,\nu) = \frac{\alpha^{\nu}.r_i^{\nu-1}.e^{-\alpha r_i}}{\Gamma(\nu)}. \quad (2)$$

In a first stage, we had to estimate the mean and variance of the gamma distribution, and in a second stage, to deduct the Empirical Bayesian Estimates of the SIR given by,

$$\hat{r}_i = \frac{y_i + \hat{\nu}}{e_i + \hat{\alpha}}. \quad (3)$$

The marginal probability of y_i (given α and ν), for an area with an expected number of cases $e_i.r_i$, where r_i is chosen at random from a gamma distribution, follows a negative binomial distribution. This may be used to derive the log-likelihood function of the parameter of the gamma

distribution: mean μ and variance τ^2 (see Eq. (2)). The log-likelihood function of the negative binomial distribution is,

$$L(\mu,\tau^2)=\sum_{i=1}^{nug}\left[\ln\left(\frac{\Gamma\left(y_i+\frac{\mu^2}{\tau^2}\right)}{\Gamma\left(\frac{\mu^2}{\tau^2}\right)}\right)+\frac{\mu^2}{\tau^2}\ln\left(\frac{\mu}{\tau^2}\right)-\left(y_i+\frac{\mu^2}{\tau^2}\right)\ln\left(e_i+\frac{\mu}{\tau^2}\right)\right]. \quad (4)$$

We can assume that μ is equal to 1, a reasonable value for the mean because the expected numbers of BSE cases e_i were based on the total WF region [16]. It is simpler to compute the log-likelihood function L for a set of values of τ^2, and to find directly which value $\hat{\tau}^2$ maximises L.

The further stage was to quantify the spatial heterogeneity of the BSE cases. Martuzzi and Hills [16] considered the variance τ^2 of the gamma distribution as a quantitative estimation of the summary of the amount of heterogeneity and the null hypothesis $\tau^2 = 0$ can be tested using a likelihood ratio test. This spatial heterogeneity test uses as a statistic, minus twice the difference λ between the likelihood value under the null hypothesis (variance equal to $\hat{\tau}^2$) and under the alternative hypothesis. In this context, λ follows a χ^2 distribution with one degree of freedom. These statistical analyses were performed with Splus® and the geographical representations were performed with ArcView®.

2.2.2. Clustering analysis

Two clustering methods were used in order to search for any geographical aggregation of BSE cases in WF.

The first method was the spatial scan statistic described by Kulldorff and Nagarwalla [14] and implemented in SaTScan® software (URL: http://dcp.nci.nih.gov/bb/satscan.html). The method draws a circular window centred on each of the area's centroid; in our analysis we used the centroids of the "communes". Then, the radius of each circle was set to vary continuously from zero to an upper limit (less than 50% of the total area). The scan method tests the null hypothesis that cattle within a particular window have the same risk of being BSE-positive than cattle outside the window. The "most likely cluster" was that with the largest likelihood ratio. The statistical significance of this largest likelihood was assessed by determining its distribution under the null hypothesis through Monte Carlo simulation (1 000 random replications of the data set generated under the null hypothesis) [6]. The analysis was performed without standardisation on the production type of cattle, dairy versus beef cattle; then we verified if the results differed with standardisation.

The second clustering analysis used the method of Besag and Newell [2]. The basis is to take into account the k nearest neighbour BSE cases for each "canton" with one BSE case. Then, for each "canton" with one BSE case or more, the p-value of observing k or more cases within the neighbouring area is computed by a Poisson probability given the population at risk in the area. The analysis was repeated for different values of k. A cluster is detected if its statistical significance (with a correction of the p-value proposed by Besag and Newell) at the 5% level persisted over three values of k [6].

3. RESULTS

3.1. Descriptive data

The 526 "cantons" of WF are grouped into 12 administrative areas named "département" and analogous to counties. For each "département", the number of "cantons", as well as the demography of cattle and the incidence of BSE during the period of interest are presented in Table I.

Between August and December 2000, 84 BSE cases were detected in WF on a

Table I. Descriptive statistics on the size of the area, the cattle population and the number of BSE cases in the 12 "départements" of western France.

"Département"	"Cantons" (Nb.)	Area (km^2)	Cattle population		BSE cases	
			Dairy	Suckling	Dairy	Suckling
Calvados (14)	49	5 609	117 932	55 668	3	0
Côtes-d'Armor (22)	51	6 991	197 999	44 075	16	0
Finistère (29)	48	6 767	176 924	37 970	10	1
Ile-et-Vilaine (35)	48	6 840	245 242	38 313	5	0
Loire-Atlantique (44)	49	6 909	127 219	74 886	5	0
Maine-et-Loire (49)	42	7 229	96 413	115 285	7	0
Manche (50)	55	6 013	262 648	47 342	4	0
Mayenne (53)	32	5 213	174 894	75 948	12	0
Morbihan (56)	40	6 879	161 205	27 022	7	0
Orne (61)	43	6 149	118 612	64 545	3	1
Sarthe (72)	37	6 245	66 519	64 782	5	0
Vendée (85)	32	6 770	8 3784	162 045	2	3
Total	526	77 614	1 829 391	807 881	79	5

population at risk of roughly 2.6 million cattle. The specific incidence was 43 BSE cases per million dairy cattle and 6 BSE cases per million suckling cattle.

Figure 1 shows the incidence of BSE in WF in the period studied. The number of BSE cases varied largely between "département". In decreasing order, the "département" of Côtes-d'Armor (No. 22), Mayenne (No. 53) and Finistère (No. 29) had the highest number of cases. Together, they represent 25% of the "cantons" of WF and 46% of the cases for 27% of the cattle population. The more populated "département", la Manche (No. 50) with 12% of the population (5% of the surface), was one of the less affected ones with only 4 cases. Lastly, the least populated "département", la Sarthe (No. 72) with 5% of the population, presented 5 cases and was the only one with 3 BSE cases concentrated in the same "canton".

3.2. Mapping analysis

The SIR are shown on Figure 2. With a mean value of the Gamma distribution of r_i fixed to 1, the variance was assessed to $\hat{\tau}^2 = 0.491$ by maximising the log-likelihood function (Eq. (4)). Values of estimated SIR were performed with equation (3). Only one "canton" had a SIR significantly higher than one (coloured in black on Fig. 2). SIR ranged from 0.80 to 2.18.

In order to test the null hypothesis $\tau^2 = 0$ (the variance of the Gamma distribution) we used the difference between the values of the likelihood function $\lambda = 9.6$ and found a p-value of 0.002. So, the SIR had a significant heterogeneous spatial distribution in WF during the study period.

3.3. Clustering analysis

Although not significant at the threshold p-value of 5%, two spatial clusters were detected with the spatial scan statistics of Kulldorff and Nagarwalla [14] (p-values of 0.052 and 0.058). Figure 3 shows these clusters and the spatial distribution of the BSE cases. The first cluster, centred on the "département" No. 22 (45 km radius), contained 18 observed BSE-cases to be compared to 6 expected BSE cases. The

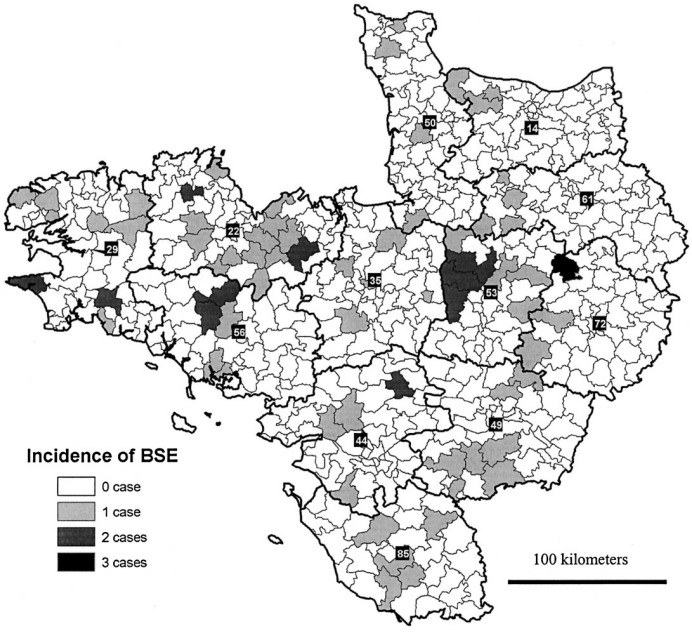

Figure 1. Incidence of bovine spongiform encephalopathy in western France ("canton" level) between August and December 2000.

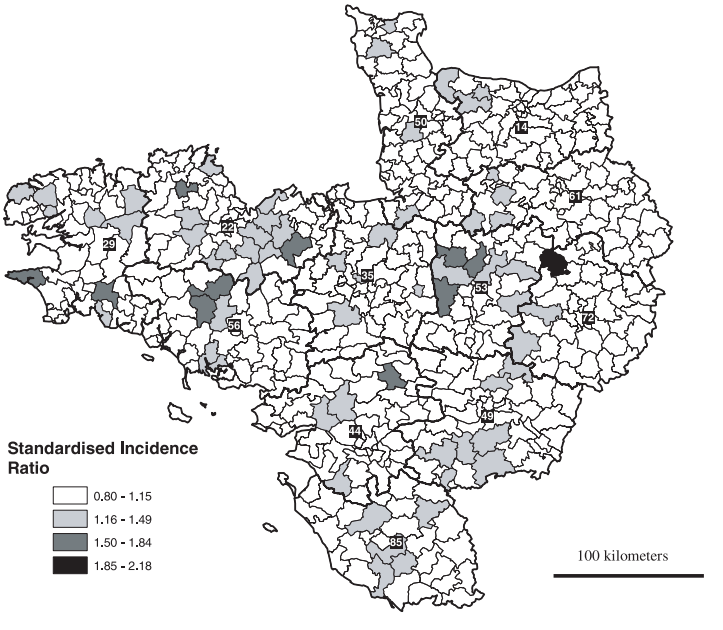

Figure 2. Standardised incidence ratio of bovine spongiform encephalopathy in western France between August and December 2000.

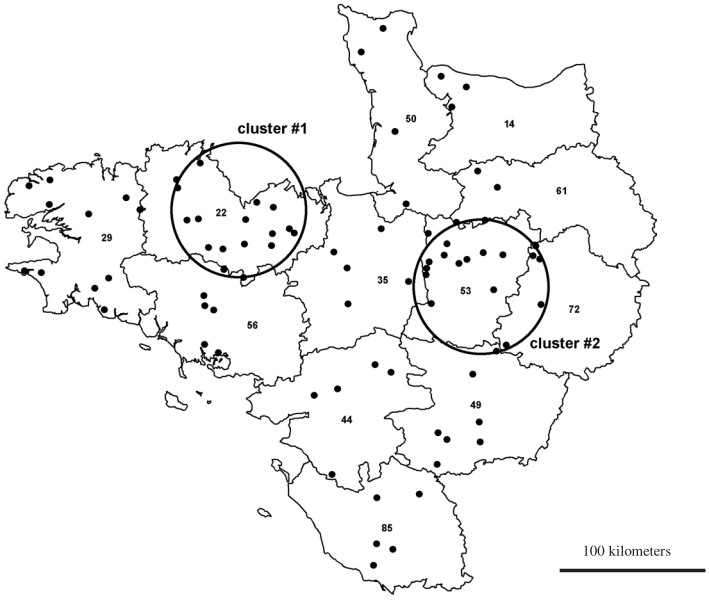

Figure 3. Spatial distribution of the 84 bovine spongiform encephalopathy cases (black dots) in western France between August and December 2000. Two clusters appeared with the method of Kulldorff: Cluster #1: 18 observed cases and 6 expected; 45 km radius. Cluster #2: 18 observed cases and 7 expected; 44 km radius.

incidence of BSE in this "département" is the greatest, 66 BSE cases per million cattle. The second most likely cluster was centred on "département" No. 53 (44 km radius) with 18 observed BSE cases for 7 expected cases. The standardisation of the analysis on the production type — dairy versus beef — gave the same results; the centroid and the *p*-value of the clusters were similar (data not shown).

The cluster analysis with the Besag and Newell method [2] evidenced 3 clusters (Fig. 4). They were the sum of several sub-clusters. Stable sub-clusters have been detected with a significant level of 5% for the values of $k = 8, 9$ and 10 BSE cases. The main one (70 "cantons" – 10 000 km^2) was observed on the "département" of Côtes-d'Armor (No. 22) and Morbihan (No. 56) and contained 20 BSE cases. The second one (38 "cantons" – 6 100 km^2) was centred on the "département" of Mayenne (No. 53) and contained 18 BSE cases. Finally another cluster, not highlighted by the Kulldorff and Nagarwalla method, appeared in the "département" of Finistère (No. 29); it grouped 29 "cantons" (4 000 km^2) and contained 9 cases.

4. DISCUSSION

Our paper presents the first spatial analysis of BSE in France. This degenerative disease is very rare, so several analysis methods have been tested in order to describe the epidemiological data as well as possible. The present work puts in evidence a significant spatial distribution heterogeneity of the BSE cases and different clusters of cases. We discuss mainly the data used for the analysis, the choice we made for the a priori information on the spatial distribution of the risk and for the Bayesian method, and the results obtained with the different statistical approaches.

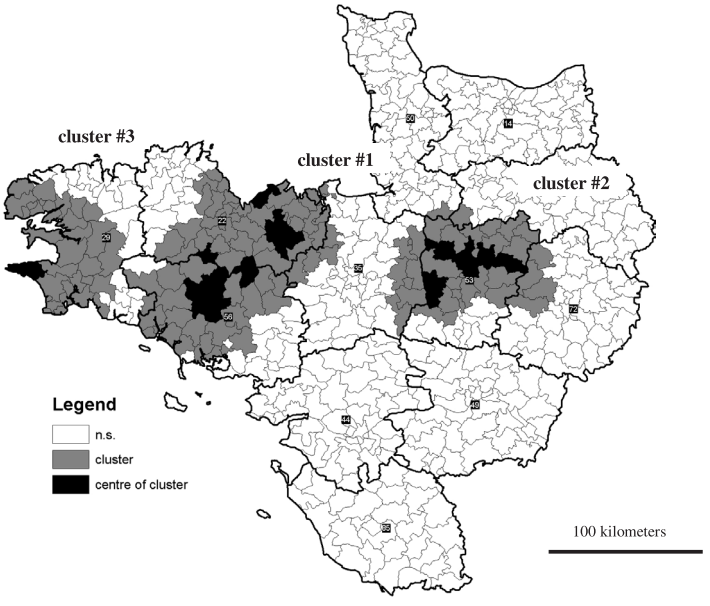

Figure 4. The three BSE clusters detected by the Besag and Newell method (p-value 5%) in western France between August and December 2000. The centers of significant clusters are in black. Cluster #1: 70 "cantons" (10 000 km^2), 20 BSE cases – cluster #2: 38 "cantons" (6 100 km^2), 18 BSE cases – cluster #3: 29 "cantons" (4 000 km^2), 9 BSE cases.

4.1. Epidemiological data

The period (August to December 2000) and the area (WF) of interest were justified by the requirement to work on comparable epidemiological data on BSE incidence; this condition was fulfilled in this period and area thanks to a pilot active surveillance program with the rapid tests. However, the consequence of studying a rare disease during a short period of time and on a limited geographical area is that we observed a few number of BSE cases; we only had 84 BSE cases, that was one case per 30 000 adult cattle. The location of the BSE cases was based on the natal holding. In our data, the cases spent their whole lives on the same farm until death except for one case that remained in the same "commune".

The main difficulty that relates to a very low disease incidence is the choice of the geographical scale. We chose the "canton", that divided the WF region into 526 geographical units, each covering on average 0.2% of the total surface. At this scale, we observed a BSE case on 71 geographical units only during the period of interest, i.e. one observation in 15% of the "cantons". The choice of such a scale was a compromise between good geographical precision, moderate demographic heterogeneity and statistical power of the analysis. Other scales such as the "département" (8.3% of the total surface) or the "arrondissement" (2.3% of the total surface), presented a poor geographical precision. Thus, they were not retained for the analysis. On the contrary, the geographical scale of the "commune" (0.02% of the total surface) was not used because we did not have demographic data for the "commune" with less than three stockholders. Moreover, the large number of communities without a BSE case did not permit the statistical analysis. In order to test a different scale and compare the results

obtained, we reran the analysis on the arrondissement scale (43 spatial units in western France). On that scale, the SIR did not have a significant heterogeneous spatial distribution (p-value 0.097) and no "arrondissement" had a SIR significantly higher than one. We found that the "arrondissement" with the highest SIR covered the area that has been evidenced at risk for BSE at the canton level, both with the mapping and clustering analyses.

The geographical heterogeneity of BSE has been studied as the first stage of a study on the factors of contamination by the BSE agent, with the underlying hypothesis that we can search for the presence of risk factors of contamination in areas with an increased risk of BSE. This makes sense if the contamination period of the cases is roughly the same. The date of birth of the 84 BSE cases was between the second semester of 1993 and the first semester of 1996 for 94% of the cases. If we consider that the contamination occurs mostly in the two first years of life [1], we can make the assumption that most of the BSE cases studied in the paper were contaminated during the same period, between 1993 and 1996. Since we took into account the location at birth, the spatial heterogeneity of the cases evidenced in our study refers to a spatial variation in the contamination risk during that period.

4.2. Disease mapping

The small number of BSE cases has some consequences on the adjustment of the Poisson model. The likelihood method, that is classically used to estimate the SIR, generates an over-dispersion [17]. Furthermore, the estimator over or underestimates the risk, especially when there are few observed cases, and the disease map results are not easily interpretable. To overcome this problem, we estimated the SIR with a Bayesian method allowing a smoothing of the estimators, in order to attenuate the contrasts artificially created by over-dispersion. With this smoothing method, we had to choose an a priori information about the SIR distribution and two types of information were available. The first type was formulated as a model with a spatial structure like Gaussian autoregressive models [3]. This takes into account the adjacency between cantons. However, the observed BSE cases are generally isolated without cases in adjacent "cantons" (see Fig. 1) and the SIR estimators of this model provided uninterpretable maps (results not shown). As a consequence, the low number of cases imposed an a priori information without a spatial structure. Therefore, we chose the Gamma distribution for the probability law of the SIR [17].

The map of the SIR (Fig. 2) highlighted contrasts between "cantons" on the basis of the risk of BSE contamination. The analysis took into account the demographic variations of the population at risk by differentiating dairy from beef cattle. The SIR was close to 1 for the "cantons" without any case. The reason is that the mean μ of the probability Gamma law was fixed at 1 and, as a consequence, the α and ν parameters were equal in the estimator [3]. Moreover, the expected number of cases remained often small (mean 0.2 cases) compared to the parameter estimations of the probability Gamma law (α and ν were approximately equal to 2). In our data, 86.5% of the "cantons" had no observed case and the median risk was 0.95. So, we observed a left imbalance on the SIR distribution (75% of the "canton" had a SIR between 0.80 and 0.99 and 25% between 1.00 and 2.18). A parallel can be made between the SIR map (Fig. 2) and the incidence map (Fig. 1).

Consequently, the risk was lower than 1 for the "cantons" without any case, higher than one for the "cantons" with one or two cases and more than twice for the "canton" with three BSE cases (Sarthe No. 72). Visually, two groups of cantons were put in evidence. The first one concerned a part of the "département" of Mayenne (No. 53) with 7 cantons at risk. The second, with

14 cantons at risk, was over the departments of Côtes-d'Armor (No. 22) and Morbihan (No. 56).

The test of heterogeneity, based on the variance τ^2 of the probability Gamma law, highlighted a spatial distribution of the SIR significantly different from a random distribution. Therefore, with the data between August and December 2000 and the Bayesian method, the risk of BSE contamination was closely related to the geography.

4.3. Disease clustering

The clustering scan method of Kulldorff and Nagarwalla [14] put in evidence two clusters (Fig. 3). Even if not strictly significant, these clusters were very close to the common level of statistical significance (5%); they were in agreement with the groups of "cantons" visually observed on the SIR map (Fig. 2) and corresponded to those evidenced with the Besag and Newell method (Fig. 4). The scan method gave circular clusters with radii of 45 and 44 km; their surfaces (approximately 6 000 km^2) were close to those of one "département". The cluster found with the Besag and Newell method (Fig. 4) on the "département" of Côtes-d'Armor (No. 22) and Morbihan (No. 56), was much larger than those observed with the Scan method. Moreover, a third cluster was evidenced in the "département" of Finistère (No. 29) with the Besag and Newell method only. The high sensitivity of this method with rare disease as well as the fact that it is less influenced by edge effects [6] explained the observed differences between the two methods.

D'Aignaux et al. [6] reproached to the Besag and Newell method to provide many false clusters because of multiple testing. To overcome this problem, d'Aignaux et al. [6] proposed first to consider only clusters with statistical significance (at the 5% level) that persist over three values of the number k of nearest neighbours of BSE cases [5, 6] and second to confirm the cluster by the method of Kulldorff. In our case, the third cluster detected with the Besag and Newell method was not confirmed by the method of Kulldorff, but it persisted over seven values of k. Moreover the p-values of the third cluster detected by the Besag and Newell method were very low ($p < 0.0001$) and we can reasonably consider that it is a real cluster.

4.4. Perspectives

Our study showed a significant heterogeneity in the spatial distribution of BSE cases in WF between August and December 2000. We found a higher risk of contamination in parts of the "département" of the Sarthe (No. 72), Mayenne (No. 53) and Côtes-d'Armor (No. 22) compared to the rest of WF. Previous works already highlighted such spatial heterogeneity, in Great Britain [21] and Switzerland [9].

The fact that BSE is a rare disease and that we worked on a short time window created difficulties in describing the spatial description of the risk of contamination. The association of several techniques of mapping and clustering was interesting in this case, since they complemented each other in the analysis of the geographical heterogeneity. In particular, the clustering technique of Besag and Newell was the most sensitive method. The clusters identified with the StatScan method were not significant at the p-value of 0.05 (0.052 and 0.058), and we can only conclude to a tendency. This might be due to the lack of power of the study, the time window being short and the number of BSE cases limited. However, the fact that the other methods showed the same aggregates of BSE cases (both significant with the Besag and Newell method, one "canton" with a SIR significantly higher than one with the mapping technique) reinforces the point that the observed clusters were not false positives.

The clustering of the BSE cases at the level of the birth farm can be due to a heterogeneity in the exposure to the BSE agent, whatever the source of this infection

risk. However, other reasons might explain the geographical clustering of the cases. First, differential surveillance between areas could provoke a spatial clustering of the disease. This was definitely taken into account by focusing the study on a period when the surveillance was accurately comparable between areas. If the clinical surveillance was not equally efficient in every area, the test of the fallen-stock animals allowed to check every animal that succumbed to BSE without being suspected of the disease. Since BSE is always a fatal disease, the surveillance system allowed to detect all animals that reached the clinical stage of the disease. Another explanation of the spatial clustering could be geographical variations of the culling curve of cattle. If the age at culling was lower in a given area, this would imply that cattle cannot reach the end of the incubation period so the probability to detect a case is lowered, even with the same infection rate. This is not the case in practice. The only variation comes from the production type of cattle, dairy versus beef.

Dairy cows are culled earlier than beef cows. This difference has been taken into account in our analysis by categorising the data according to the production type.

In conclusion, we evidenced a link between the geographical location and the risk of BSE contamination in WF. Given the lack of power of the study, the precise location of the areas with a higher BSE risk has to be considered as tendencies. The following stage is to expand the analysis to the rest of the French territory to reinforce the statistical power of the data and to explore the different reasons that explain the geographical heterogeneity of the BSE risk.

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