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► To cite this version:

Anne Buschmann, Franz J. Conraths, Thomas Selhorst, Julia Schultz, Matthias Kramer, et al..
Imported and indigenous BSE cases in Germany. *Veterinary Microbiology*, 2007, 123 (4), pp.287.
10.1016/j.vetmic.2007.04.011 . hal-00532244

HAL Id: hal-00532244

<https://hal.science/hal-00532244>

Submitted on 4 Nov 2010

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Accepted Manuscript

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PII: S0378-1135(07)00165-4

DOI: doi:10.1016/j.vetmic.2007.04.011

Reference: VETMIC 3642

To appear in: *VETMIC*



Please cite this article as: Buschmann A., Conraths F.J., Selhorst T., Schultz J., Kramer M., Groschup M.H., Imported and indigenous BSE cases in Germany, *Veterinary Microbiology* (2007), doi:10.1016/j.vetmic.2007.04.011

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Imported and indigenous BSE cases in Germany

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Abstract

Bovine spongiform encephalopathy (BSE) is a transmissible fatal neurodegenerative disease in cattle with an average incubation time of approximately 5 years. The first BSE case in an indigenous cow was detected in Germany in November 2000. This was almost eight years after the huge BSE epidemic in the United Kingdom had peaked, and several years after many EU member states had seen their first BSE case. In the 1990s, BSE had been diagnosed in six import animals in Germany. However, after the implementation of an active surveillance programme using BSE rapid testing systems, 399 indigenous German BSE cases have been found up to the end of July 2006. The birth cohorts of 1995-1997 contribute to the vast majority of the first two hundred and fifty German cases that were diagnosed between 2000 and 2003. However, the most recent German BSE cases belong primarily to the birth cohorts 1998-2000 which is indicative of a recycling of BSE infectivity at that time. Moreover, there were two BSE cases in cattle born in spring 2001, i.e. after the meat and bone meal feed ban had come into effect on January 1st, 2001. In this article, we describe the dynamics of the German BSE epidemic and compare these data with those of other countries that observed larger numbers of cases.

Keywords: BSE epidemic, bovine spongiform encephalopathy, surveillance

1. The BSE epidemic in the United Kingdom and elsewhere

The first BSE case was diagnosed in the UK in 1986. Case control studies carried out in 1988 finally revealed that this disease is transmitted by feeding infectious meat and bone meal (MBM) to cattle (Bradley, 1991; Bradley and Wilesmith, 1993). Despite the immediate prohibition of this practice, the extremely long incubation time led to a peak in the British BSE epidemic in the years 1992/93. Additionally, since the initial feed ban was not strict enough, two further reinforcements were needed in 1994 and finally in August 1996. After

that it can be assumed that new BSE infections have not occurred in the UK - at least on a large scale. From then on all specified risk material (SRM; tissues harbouring or believed to contain BSE infectivity in infected animals) had to be removed from all slaughter animals and fallen stock and effective measures were taken to destroy it. All MBM produced from this material was prohibited from exportation to other EU countries and was therefore increasingly exported to non-EU countries (Figure 1). Almost simultaneously, more and more BSE cases (albeit on a much smaller scale) were found in other EU member states including Ireland, France, Portugal and Switzerland¹. Similar measures were taken in these countries based on their national legislation in order to prevent further infections in bovines. This is presumably the reason why most of the past and current BSE cases in the EU15 (European Union with 15 member states, until 30th April 2004) were born in the years before effective measures were taken, i.e. belong to birth cohorts 1995/96 and before. However, the occurrence of the more than 130 'Born after the reinforcement of the ban' (BARB) BSE cases in the UK (incl. 3 animals born in 2002) also illustrate how difficult the implementation of such measures is.

2. German BSE surveillance and import cases before 2000

Germany belongs to the group of EU member states in which the first indigenous BSE case was detected after 2000 and where a considerable number of cases have been discovered after the implementation of an active BSE surveillance programme. Germany had not previously implemented effective surveillance measures, making the epidemiological situation slightly different to that of other member states with early BSE cases.

The BSE cases in imported animals that were diagnosed before 2000 were all detected by passive surveillance measures in imported animals based on clinical signs indicative of a neurological disorder. The first case was confirmed in a mouse bioassay in January 1994 for a Scottish Highland breed animal that had been imported from the United Kingdom (UK) and

¹ for details see http://www.oie.int/eng/info/en_esbincidence.htm

77 had already died on a farm in Schleswig-Holstein in February 1992. The second case occurred
 78 in February 1994 in a Galloway cow imported from the UK that had been euthanised in
 79 Lower Saxony, while the third case was diagnosed in May 1994 in a Welsh Black breed
 80 animal that was also imported from the UK and euthanised in Lower Saxony. The next case
 81 was diagnosed in a Hereford breed animal that died at the University of Veterinary Medicine,
 82 Hanover, Germany, in April 1994 where it was being treated for lameness. The diagnosis of
 83 these three cases in 1994 was perhaps a consequence of the official confirmation of the first
 84 BSE case in an imported animal at the beginning of the same year (see above). Because of the
 85 increased awareness, histopathological examinations by state regional laboratories were
 86 intensified for UK import animals (a total of around 9,000 animals), in particular if they had
 87 suffered from neurological disorders or had died without another plausible reason. The fifth
 88 BSE case in Germany was found in a Galloway cow originating from the UK that died on a
 89 farm in North Rhine-Westphalia in January 1997. Finally, one case was diagnosed in
 90 September 1997 in a Simmentaler Fleckvieh cow that had been imported from Switzerland
 91 and euthanised in Bavaria in May 1997. The final positive or negative confirmation of a
 92 suspected BSE case was given by the National Reference Laboratory (NRL) at the Friedrich-
 93 Loeffler-Institut (formerly known as 'Bundesforschungsanstalt für Viruskrankheiten der
 94 Tiere' – Federal Research Institute for Viral Diseases in Animals). The laboratory prepared
 95 the scrapie-associated fibrils (SAF) and then used immunoblotting in line with an OIE-
 96 approved protocol originating from the EU reference laboratory at the Central Veterinary
 97 Laboratories (now Veterinary Laboratories Agency) in Weybridge, UK.

98 After the first BSE rapid tests had been developed, a pilot study of 5,029 healthy
 99 slaughtered cattle was carried out in North Rhine-Westphalia using the Prionics Check
 100 Western Test (Prionics AG, Schlieren, Switzerland). This study included animals from all
 101 geographical origins and breeds and was designed to evaluate the practicability of rapid
 102 testing and assess the local BSE situation, albeit on a very small scale. The fact that no

positive case was found during this study reassured some veterinary authorities and politicians that the BSE risk in Germany was very low or even non-existent.

3. The indigenous German BSE cases in 2000-2006

Prior to a random rapid testing programme of cattle that was scheduled to start in April 2001 following the decision made by the commission 2000/374/EG, a voluntary testing programme was initiated in Germany in November 2000. On the second day of testing in a private laboratory, this led to the detection of the first indigenous German BSE case in a healthy slaughter animal of 51 months of age from Schleswig-Holstein. The BSE case was confirmed by the NRL on November 27th, 2000. After this discovery, the routine testing of all healthy slaughter animals over 30 months of age (reduced to 24 months in January 2001 after the discovery of two German BSE cases in 28-month-old animals that had been tested voluntarily) as well as of all risk animals over 24 months of age was implemented from January 1st, 2001 in line with EU regulation 999/2001 and amendments. At first, there were only two rapid tests available (Prionics Check Western test and the BioRad PLATELIA test (now TeSeE)). Eventually, six additional rapid tests were approved by the EU and the national authorities: Enfer TSE test (national approval 8/2002), Prionics Check LIA test (national approval 7/2003), IDEXX HerdCheck Test (national approval 4/2005), BetaPrion BSE EIA Test Kit (national approval 6/2005), the Prionics-Check PrioSTRIP test (national approval 6/2005) and the PrionScreen test (national approval 2/2006). The total number of BSE rapid testing laboratories in Germany was initially over 100 but had decreased to 32 by May 2006.

In the five years after the implementation of the active BSE surveillance programme, almost 12 million slaughter animals were rapid-tested and 181 BSE cases have been detected (Table 1). This represents an incidence of 15.6 BSE cases per million slaughter animals over five years. However, more than two million of the 11.6 million bovines were under 24 months

of age and tested voluntarily, all with negative results. On the other hand, rapid testing of more than 1.2 million risk animals yielded 207 BSE cases. This clearly marks a more than tenfold higher incidence (166.1 cases per million tested animals) as compared to the group of healthy slaughter cattle. Altogether, 399 indigenous BSE cases were found in Germany by the end of July 2006 and the rate of incidence has decreased more or less steadily over the last five years (7 cases in 2000, 125 in 2001, 106 in 2002, 54 in 2003, 65 in 2004, 32 in 2005 and 10 up to the end of July 2006).

It is worth noting that despite intensive training of veterinarians, farmers and other cattle handlers, only 34 German BSE cases were initially recognized as suspect animals because they showed clinical BSE-like symptoms (plus four cases in BSE cohorts that displayed clinical symptoms). Moreover, the percentage of clinically suspect cases that were later confirmed fell from 14.4% in 2001 to 4.6% in 2004 and 0% in 2005. However, three clinical suspect cases were confirmed as BSE positive in 2006, which represents 30% of all cases diagnosed up to the end of July (Table 2). This finding is in contrast to other European countries where a higher ratio of confirmed BSE cases was initially notified as clinically BSE suspect. The percentage of BSE cases in healthy slaughter animals increased over the years (31.2% in 2001, 60% in 2004, 56.3% in 2005, and 40% in the first 7 months of 2006), while the relative contribution by risk animals (excluding clinical suspects and cohort cases) fluctuated (51.2% in 2001, 32.3% in 2004, 43.7% in 2005 and 30% in January - July 2006 (Table 2)).

In total, 10 BSE birth and feeding cohort cases were identified in a second animal of the same herd (Table 3), which is indicative of an elevated risk of a BSE infection in this group.

Most interestingly, the age and birth structure of the German BSE cases changed quite remarkably over time. In the first two years, more than 80% of the diagnosed BSE cases belonged to the birth cohorts of 1995 and 1996 and the age of the infected animals increased

accordingly from 65 months in 2001 to 76.8 months in 2002. BSE cases diagnosed in 2003 were spread equally among the birth cohorts of 1995 to 1999 and the mean age decreased to 73.8 months. A clear shift to the birth cohorts of 1999 and 2000 became evident in the year 2004 when the birth cohort of 1999 contributed the largest number of BSE cases and the mean age rose to 75.3 months (Figure 2). This trend continued in 2005 while the mean age simultaneously dropped to 72.3 months. In 2006, nine out of the ten cases diagnosed in the first seven months belonged to the birth cohorts 1999 and 2000. Taken together, the majority of BSE cases were born in the years 1995 and 1996 and the number of new BSE infections in German cattle seems to have considerably decreased in the period from 1997 to 2000, although Germany had not implemented any of the new regulations for the prevention of further BSE infections in 1996. A similar development was observed in almost all other EU member states (Anonymous, 2004). It is tempting to speculate that the development in Germany might have been indirectly affected by the introduction or reinforcement of the MBM feed and exportation bans in other countries.

As 23 BSE cases have already been diagnosed from the birth cohort of the year 2000, more cases from this birth cohort must be anticipated. The first BSE case of this birth cohort was diagnosed in March 2004 and animals born in 2000 comprised 15.4% of all BSE cases diagnosed in that year. For 2005, animals of this birth cohort represent 25.8% of all BSE cases and 50% of the cases diagnosed in the first seven months of 2006. In April 2005, BSE was diagnosed for the first time in an animal born in May 2001, which was after the implementation of the feed ban in December 2000. A second case followed in June 2005 when BSE was diagnosed in an animal that had been born in March 2001. This indicates that, despite the total feed ban, residual BSE infectivity was still circulating in the cattle feed chain five months later. The specific origin of these two BSE cases is currently under thorough epidemiological investigation.

4. Lessons to be learned

The almost immediate discovery of an indigenous BSE case after the start of the BSE rapid testing programme in November 2000 and the comparatively large number of BSE cases diagnosed since then strongly indicate that BSE cases in German cattle had been occurring for several years before this date. And equally, based on the current epidemiological data, it can be predicted that the German BSE epidemic will last longer than it would have, if an efficient surveillance system had been established before 2001 and effective measures against the contamination of cattle feed with BSE infectivity had been taken. After the detection of the first BSE cases, it turned out that the grouping of Germany into the geographical BSE risk (GBR) group III (BSE infection of indigenous cattle is probable, but not confirmed; Anonymous 2000) was indeed correct.

Despite the six BSE cases in imported animals, which were discovered by passive surveillance, only the implementation of an active surveillance programme led to the detection of the indigenous BSE cases that must have been present in the German cattle population for a considerable time beforehand. Therefore, the implementation of an active surveillance system is a crucial factor for the assessment of the disease epidemiology within a country and thus enables effective consumer protection. The surveillance system must be based on rapid tests that have been approved for the screening of cattle samples and that display an adequate diagnostic sensitivity and specificity. This was already the case when the active surveillance programme started, but it has been constantly improved by amendments of the already available tests as well as by the extension of the list of approved rapid tests.

Another crucial point for stopping BSE infection in the cattle population is effective legal regulation to prevent infections by feeding stuff. Such measures were only taken in December 2000 in Germany. It is widely acknowledged that the BSE agent was distributed among the cattle population through the oral uptake of BSE-contaminated feedstuff that contained MBM (Wilesmith et al., 1988). Moreover, the feeding of infectious milk replacers

has been suspected as a transmission route in the German BSE epidemic (Kamphues et al., 2000). This has been confirmed for Bavaria (Clauss et al., 2006) and Schleswig-Holstein (Pottgiesser et al., 2006).

Although it had been widely acknowledged that there was only one single BSE strain present in the worldwide cattle population, the recent detection of two different forms of atypical BSE first in France and Italy (Biacabe et al., 2004, Casalone et al., 2004), and later also in Germany (Buschmann et al., 2006) and other member states in a small number of cases, has proved that this assumption was wrong. Even though the zoonotic potential of these newly discovered forms still needs to be evaluated the first lesson to be learnt from this discovery is that researchers as well as veterinary authorities must remain aware of the possibility of novel and unexpected developments in the field of transmissible spongiform encephalopathies.

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Table 1: BSE rapid tests carried out in Germany: 2001 - 2005¹

Year	2001	2002	2003	2004	2005	Total
Healthy slaughtered cattle < 24 months	420,776	763,850	503,183	366,365	54,231	2,108,405
24 – 30 months	654,050	339,520	280,800	265,689	245,454	1,785,513
30 – 96 months	1,477,811 ²	1,510,135	1,303,815	1,355,656	1,293,658	6,946,075 ²
> 96 months	²	154,453	244,848	258,526	246,369	904,196 ¹
Age unknown	40 623	9,166	4,593	2,646	654	57,682
Total healthy slaughtered cattle	2,593,260	2,767,958	2,337,239	2,248,882	1,840,366	11,787,705
Risk animals ³ < 24 months	5,713	7,834	7,356	6,088	3,030	30,021
24-30 months	87,109	30,802	26,976	26,395	25,629	196,911
30 – 96 months	135,499	195,858	187,277	173,496	173,322	865,452
> 96 months	²	25,368	30,924	31,546	32,694	120,532
Age unknown	47,417	2,724	1,399	766	243	52,549
Total risk animals	275,738	262,586	253,932	238,291	234,918	1,265,465
Total tested animals	2,868,998	3,030,544	2,591,171	2,487,173	2,075,284	13,053,170

¹. = figures for Nov/Dec 2000 are not available² = for 2001, animals over 30 months of age were taken as one group without further differentiation³ = risk animals include fallen stock, emergency and sick slaughter, clinically suspect animals, and cohort culling.

262 (Source: Federal Ministry of Nutrition, Agriculture and Consumer Protection (BMELV))

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Table 2: Numbers and percentages of BSE cases per year

In this table, clinically suspect cases and cases from cohort culling are excluded from the group of risk animals and are counted separately

Year	2000	2001	2002	2003	2004	2005	2006 (Jan-July)	Average percentage
Healthy slaughtered cattle	5 (71.4%)	39 (31.2%)	49 (46.2%)	31 (57.4%)	39 (60.0%)	18 (56.3%)	4 (40%)	51.8%
Risk animals ¹	1 (14.3%)	64 (51.2%)	45 (42.5%)	20 (37.3%)	21 (32.3%)	14 (43.7%)	3 (30%)	35.9%
Clinically suspect animals	1 (14.3%)	18 (14.4%)	8 (9.4%)	2 (3.7%)	3 (4.6%)	0 (0%)	3 (30%)	10.9%
Cohort animals	0 (0%)	4 (3.2%)	3 (2.8%)	1 (1.9%)	2 (3.2%)	0 (0%)	0	1.6%
Total	7	125	106	54	65	32	10	-

Table 3: German BSE cases in cohort animals

Cohort No	No of animals in affected herd	Federal State where case occurred	Age of first case (months)	Age of cohort case (months)
1	101	Schleswig-Holstein	51	59
2	952	Saxony-Anhalt	55	58
3	37	Baden- Württemberg	58	57
4	75	Bavaria	57	56
5*	2,946	Saxony	57	54
6	66	Bavaria	61	62
7	100	Baden-Württemberg	58	52
8	50	Baden- Württemberg	52	52
9	155	Lower Saxony	102	102
10	105	Bavaria	67	73

* Another BSE case was found in this large cattle herd three years after the index case, but not in an animal belonging to the initial birth cohort

Figure legends:**Figure 1: UK exports of MBM: 1979-1995**

(Source: <http://www.bseinquiry.gov.uk/report/volume10/chaptef2.htm#274058>)

Figure 2: Year of birth (a) and ratios (b) of the German BSE cases diagnosed between 2000-2005