Bovine Spongiform Encephalopathy (BSE)

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EPIDEMIOLOGY

Spatial and temporal distribution of BSE

Detailed tables containing information on countries in which BSE has been reported are provided by the World Organisation for Animal Health (OIE) on its website (BSE specific data – www.oie.int). Apart from the 184,169 cases in cattle that were diagnosed in the UK up to the end of 2011, 20 other European countries also recorded the disease, some such as Portugal, Switzerland and Ireland at high prevalence rates. However, only four countries outside Europe reported cases that were not imported, viz. Canada, Israel, Japan and USA. No locations in the southern hemisphere have reported indigenous cases of BSE.

A table reflecting the ‘annual incidence rate’\(^1\) of BSE in individual countries is provided on the OIE’s website (www.oie.int). This shows that by the end of 2011 only twelve countries, including UK, still had an annual incidence rate above zero. With the exception of Canada all these countries are in Europe. These data are likely to be reasonably accurate because no other disease enjoys the intensity of surveillance accorded to BSE in Europe. For example, throughout the European Union (EU), all cattle over the age of 30 months slaughtered for human consumption are currently tested for BSE using modern laboratory methods. The likelihood of BSE entering the human food chain in the EU is consequently close to zero.

A comparison of the epidemic curves of BSE and vCJD in the UK is shown in Figure 1. The time differences between the peaks of the BSE and vCJD epidemic curves (1992 & 2000 respectively) are explained by the infection affecting people only once the bovine epidemic had picked up momentum and the incubation period of vCJD being even longer than for BSE. The long ‘tails’ of the epidemic curves have not yet been reliably explained but probably relate to a minority of cases having exceptionally long incubation periods. Nevertheless, it can be predicted with reasonable assurance that BSE and vCJD will become historic in Europe in the next few years.

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\(^1\) The number of indigenous cases per 1 million cattle over the age of 24 months
Species and PrP<sup>Sc</sup> strain associations

The vast majority of BSE cases that made up the European pandemic were caused by a single strain of PrP<sup>Sc</sup> (assessed on the basis of mouse biological tests; Bradley & Verwoerd, 2004b). Rare cases of BSE were identified in Europe that were caused by different strains. Recently PrP<sup>Sc</sup> ‘types’ have been differentiated on the basis of their molecular mass. In addition to the predominant type associated with the European pandemic (designated C), small numbers of cases with a lower (designated L-type) or higher (H-type) molecular mass were identified. In 2011 two BSE cases were found in Switzerland with a novel molecular weight, i.e. different from C-, H- and L-types (http://escope.prionics.com/issue/2011-decemb).

Apart from cattle, a few cases of BSE also occurred in antelope and bison in zoos as well as a number of felid species that were fed on rations that contained MBM (Bradley & Verwoerd, 2004c; Table 1). For many years, however, there was no evidence that BSE affected domestic ruminants other than cattle. Recently, however, two cases have also occurred in goats in Europe and sheep have been found to be susceptible experimentally (Spiropoulos <i>et al.</i>, 2011). These findings reinforce the need for control measures against BSE to be retained to prevent another epidemic because the potential is that aberrant prion proteins will continue to arise, albeit infrequently, in cattle or small stock. If these prions enter the animal feed chain where an ‘unstable’ BSE situation exists (see below), a new epidemic could potentially arise.

For the above reasons it will likely never be possible to consider BSE ‘eradicated’. This has trade implications that will be discussed below.

Table 1: Transmissible spongiform encephalopathies that affect humans and animals

<table>
<thead>
<tr>
<th>Disease</th>
<th>Natural host</th>
<th>Other hosts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scrapie</td>
<td>Sheep and goats</td>
<td></td>
</tr>
<tr>
<td>Transmissible mink</td>
<td>Mink</td>
<td></td>
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<tr>
<td>encephalopathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic wasting disease</td>
<td>Mule deer, elk &amp; white tailed</td>
<td></td>
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</tbody>
</table>

Page 2
<table>
<thead>
<tr>
<th>Disease</th>
<th>Natural host</th>
<th>Other hosts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine spongiform encephalopathy</td>
<td>Cattle &amp; goats</td>
<td>Domestic cats, captive wild felids (lions, tigers, cheetahs) and bison &amp; antelope</td>
</tr>
<tr>
<td>Variant Creutzfeldt-Jakob disease</td>
<td>Humans</td>
<td></td>
</tr>
<tr>
<td>Kuru</td>
<td>Humans</td>
<td></td>
</tr>
<tr>
<td>Creutzfeldt-Jakob disease</td>
<td>Humans</td>
<td></td>
</tr>
<tr>
<td>Gerstmann-Staüssler-Scheinker syndrome</td>
<td>Humans</td>
<td></td>
</tr>
<tr>
<td>Fatal familial insomnia</td>
<td>Humans</td>
<td></td>
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</tbody>
</table>

**Lessons from the European pandemic (1989-2011)**

The European pandemic centred on the UK has been described as an extended common source epidemic, the source being MBM containing prion protein fed to cattle (Anderson et al., 1996; Ducrot et al., 2008). The much earlier occurrence of cases and the peak incidence of cases in the UK (1992) in comparison with those of other European countries, indicates that the European pandemic probably spread from the UK to other countries (presumably mainly through export of MBM but also of live cattle in the incubation phase of the disease that subsequently entered the ruminant feed chain).

Circumstantial evidence indicated that procedures at rendering plants in the UK changed in the early 1980s, resulting in waste material from animal carcasses being heated less thoroughly than was the case previously. Additionally, a solvent extraction step was dispensed with (this was originally thought to be an important factor but later research showed the BSE agent to be little affected by the solvent concerned – Bradley & Verwoerd, 2004b). The result was increasing quantities of PrP^Sc being recycled with new cases of BSE occurring exponentially, albeit that these cases only became obvious 4-5 years later.

Although other methods of transmission of BSE have been investigated, including horizontal and vertical, none have provided conclusively positive results. It has been concluded therefore that maternal transmission either does not occur or does so at an insignificant rate (Bradley & Verwoerd, 2004b; Ducrot et al., 2008).

All breeds and both sexes of cattle appear to be equally susceptible to BSE (Bradley & Verwoerd, 2004). However, there is evidence of genetic predisposition to vCJD among people (Lewis et al., 2006).

The youngest animal so far identified with BSE was 20 months old – in the UK. Two cases below the age of 30 months were also diagnosed in other European countries but the vast majority of cases have been in cattle 30 months or older with the average age being over 5 years (Decrot et al., 2008).
The following commodities and products derived from cattle are considered by the OIE (based on extensive background research) as safe from the BSE perspective and therefore should not be associated with import restrictions applicable to BSE: blood, milk and milk products, semen, embryos, hides and skins and gelatine and collagen derived from skin, tallow and dicalcium phosphate (there are specific qualifications for some of these – see Article 11.5.1 of the Terrestrial Animal Health Code, www.oie.int).

Ducrot et al. (2008) in their review emphasized a number of findings:

- That passive surveillance is inadequate for BSE detection: only after the introduction of mandatory active surveillance in 2001 in most EU countries did the true extent of the BSE problem become apparent. Between 2001-2005 over 50 million cattle were subject to laboratory screening for BSE in European countries which identified about 7 000 cases (i.e. one case per 7 143 cattle tested). In most of these countries active surveillance consisted of a combination of (1) targeted surveillance for suspect clinical cases among downer cows, emergency slaughter animals and animals that died or were killed during transportation and older than 24 months of age, and (2) a sample (typically 3%) of slaughter cattle over 30 months of age.

- Results from extensive surveillance in EU countries identified a number of risk factors:
  - dairy cattle – beef cattle were only about 1/3 as likely to develop BSE as dairy cattle (ascribed to the fact that dairy cattle consume more formulated feeds and less grass than do beef cattle);
  - season of birth – in the UK, dairy cattle born in autumn were found to be at higher risk of developing BSE than those born in spring and in France this applied to beef cattle as well (ascribed to spring calves obtaining feed via grazing in fields while autumn calves are raised for the first few months of life in barns and fed formulated feeds exclusively);
  - dairy cows in highest producing herds had a three-fold higher risk of developing BSE than those in lowest producing herds (ascribed to high producing cows consuming more formulated feed than others);
  - the age of dairy cows at first calving; the earlier the age the greater the likelihood of development of BSE;
  - although not a universal finding, BSE appears to have been more common in large herds, possibly related to feeding practices;
  - in a number of countries there were also geographical differences between different parts of the same country, probably resulting from specific feed suppliers in different locations selling relatively highly contaminated feed;
  - inconclusive evidence was found for milk replacers based on tallow having an association with BSE cases although tallow is considered to be a safe product.

**Surveillance for BSE**

As indicated in the section above, it has been shown repeatedly in Europe that passive surveillance for BSE is inadequate for detection of the presence of BSE; therefore active surveillance is considered
essential. The OIE – which provides an accreditation system for member countries in relation to the adequacy of BSE risk control in countries (i.e. it does not certify ‘disease-freedom’ as is the case for foot and mouth disease, for example) – provides guidance on surveillance approaches and standards (Chapter 11.5 – TAHC, OIE, 2011). These standards present a problem for developing countries because the surveillance requirements for listing as a country or zone with either ‘negligible’ or ‘controlled’ risk BSE risk are logistically and financially demanding. Few African countries, even those dependent on beef exports, are in a position to fulfil the surveillance requirements advocated by the OIE because the cost of compliance far outweighs potential financial benefit. This results in a ‘catch 22’ situation where listing by the OIE as a country with negligible risk is important for market access but the costs involved would make export unprofitable. This problem is discussed further under control.

**BSE and African countries**

The issue of whether BSE presents a real risk to African countries continues to be a matter of debate. On one hand, because no indigenous cases of BSE have been identified in the southern hemisphere the risk appears to be non-existent; on the other hand, it is possible that cases were imported into some southern African countries by imports of live cattle and/or feed constituents such as MBM in the period before the extent of the BSE problem in Europe became apparent. This could, in the opinion of the European Commission (EC), be the case for South Africa, although the South African Government disputes the ‘facts’ on which this opinion rests. This disagreement arose as a result of South Africa’s application to the European Food Safety Authority (EFSA) for a GBR (Global BSE Risk) rating in 2001 and the subsequent categorization in 2003 of South Africa’s status as GBR III (i.e. likely but not confirmed that domestic cattle are infected with the BSE agent). South Africa made this application to the EFSA because the OIE at that time did not have a well-developed BSE accreditation system and the EC was providing interim international leadership. According to the South African authorities, the GBR assessment was not properly completed due to failure on the part of South Africa to supply supplementary information to the EFSA on time, i.e. the assessment was based on inaccurate data. However, this assessment is still on record and the EFSA assessed South Africa’s ‘external challenge’ (i.e. the likelihood that the BSE agent was introduced into the country) as follows:

- 1986-1990 overall – high; MBM – moderate;
- 1991-1995 overall – moderate; MBM – very low;

On balance it would appear that the rating accorded to South Africa by the EFSA was deficient insofar as MBM imports are concerned. However, there is no doubt that cattle were imported into South Africa from the UK during the early stages of the BSE epidemic in that country and that no assurance is available to show that tissues from these cattle did not enter the animal feed chain as carcass meal. If that did happen the question is whether the infection could have been maintained by carcass meal incorporated into animal feed on a repetitive basis, i.e. resulting from an ‘unstable’ BSE control system. A study conducted...
in 2010 on behalf of the Southern African Development Community (SADC) showed that management of risks associated with the manufacture and distribution of carcass meal in South Africa did not accord with international standards (Thomson, 2010). This poses a regional problem because most countries in southern Africa import cattle and feeds from South Africa.