

Editorial: The European Response to BSE: A Success Story

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*"I dread success. To have succeeded is to have finished one's business on earth...
I like a state of continual becoming, with a goal in front and not behind."
-- George Bernard Shaw*

Bovine spongiform encephalopathy (BSE, "mad cow disease") was officially first reported in November 1986 in the UK. It became quickly interpreted as likely counterpart in bovines of scrapie, the paramount transmissible spongiform encephalopathy (TSE, prion disease) in sheep and goats. A landmark epidemiological study by John Wilesmith and co-workers (Wilesmith et al., 1988) identified in 1988 cattle feedstuffs containing ruminant-derived protein (meat-bone meal, MBM) as source for the evolving epidemic that numbered almost 185.000 diagnosed cases in total in the UK and a further 5.500 elsewhere in the EU, with some 2 million infected bovines estimated to have entered the human food chain in the UK. The first UK response was a ban on feeding MBM to ruminants, as a measure that significantly curbed but did not eliminate the epidemic.

A likely link between BSE and the human disease variant Creutzfeldt-Jakob disease (vCJD) was published in early April 1996 (Will et al., 1996), followed by a media outbreak of apocalyptic scenarios sketching a man-made disaster of then unpredictable proportions. Health authorities were frantically acting to limit damage from BSE not only to human health, but also to agriculture, economies, political credibility and public confidence. In the UK, the Phillips Inquiry (Lord Phillips et al., 2000) took two and a half years to accrue insight into why and how the BSE saga developed. The key conclusions depicted BSE as a consequence of intense farming practices, with significant shortcomings in the way things were done, with sensible measures taken that were not always timely and adequately implemented and enforced, and implicitly guided by the belief that BSE was not a real threat to human health. Moreover, there was too much secrecy and unjustified reassurance by governmental bodies in order to protect the agricultural industry.

Almost simultaneously with publication of the Phillips Report, the second public BSE crisis started in 2000 when first results of active BSE surveillance on the European continent confirmed scientists' opinion that political claims of "freedom from BSE" in several countries were wishful thinking rather than reality. As a result, the EU TSE Regulation of 2001¹ laid down a comprehensive set of harmonised rules for the prevention, control and eradication of TSEs, including an EU-wide total ban on the feeding of animal proteins to farmed animals. More or less independent national food safety authorities were now established in most EU countries, and the need to separate risk assessment from risk management could no longer be ignored.

¹ Regulation (EC) No 999/2001 of the European Parliament and of the Council of 22 May 2001 laying down rules for the prevention, control and eradication of certain transmissible spongiform encephalopathies. OJ L 147, 31.05.2001, p. 1-40.

Since the first BSE crisis of 1996, the European Commission (EC) has embarked on a science-guided response, establishing a TSE/BSE *ad hoc* Group of their Scientific Steering Committee (SSC) that provided up to 2003 a plethora of opinions on all aspects of BSE and other TSEs (SSC, 1997-2003). The SSC was a risk assessment and risk advisory body, separated from risk management which remained with the EC Directorate General for Health & Consumers (DG SANCO). From December 1997, the SSC adopted their first important documents on the scientific basis to protect human health from BSE, such as the definition of tissues containing most of infectious TSE agents (prions), termed Specific Risk Materials (SRM). Regrettably, politicians in several EU Member States (MS) were then unwilling to translate this into legislation, still sticking to their “freedom from BSE” illusion. It was only after a delay of almost 3 years that the EU-wide SRM ban, the most important measure to protect public health from BSE, became implemented.

Since 2003, EFSA has taken over the role of science-based advice to the EC on BSE/TSE-related matters, with the BIOHAZ Panel producing an equally impressive amount of opinions and reports (EFSA, 2003-2011) as the former SSC. As a whole, these scientific risk assessments – first by the SCC, then by EFSA – and their translation into adequate measures by national and EC risk managers were the basis of the European response to BSE, which has been a spectacular success story. This is evident from quantitative data on both the animal and human disease. First, the prevalence of BSE as detected by current surveillance has come down steadily in the EU to a trickle, from several thousands of cases in the early 2000s, to 44 in 2010 in the EU (11 in the UK) (OIE, 2011). Second, surveillance of vCJD in the UK indicates that the epidemic, having reached a peak in the year 2000 when there were 28 deaths, has declined to a current incidence of about one diagnosis/death per year (Andrews, 2011). Clearly, it is now time to be re-assured but still too early for complacency (Budka et al., 2008).

Given the quantitative indicators of what seems, in the EU, to be the near-extinction of the animal epidemic and control of cattle-to-human transmission, is there anything left for concern? Unfortunately, there is. With BSE, the global disease burden is far from clear in countries with less well-developed surveillance. In humans, the potential continuing person to person spread by blood and blood products remains a problem as seen with the four cases of transfusion-associated vCJD infection to date (Andrews, 2011). With BSE and other TSEs in animals, the recognition of the wide diversity of prion strains in the field, including three new forms of animal TSEs (L-type Atypical BSE, H-type Atypical BSE and Atypical scrapie), has complicated disease diagnosis and surveillance, as well as scientific assessment of their potential risks to humans. EFSA and the European Centre for Disease Prevention and Control (ECDC) recently delivered a scientific opinion on any possible epidemiological or molecular association between TSEs in animals and humans (EFSA Panel on Biological Hazards (BIOHAZ) and ECDC, 2011). This opinion confirmed Classical BSE prions as the only TSE agents demonstrated to be zoonotic so far but the possibility that a small proportion of human cases so far classified as “sporadic” CJD are of zoonotic origin could not be excluded. Moreover, transmission experiments to non-human primates suggest that some TSE agents in addition to Classical BSE prions in cattle (namely L-type Atypical BSE, Classical BSE in sheep, transmissible mink encephalopathy (TME) and chronic wasting disease (CWD) agents) might have zoonotic potential. In particular the L-type Atypical BSE agent might be similarly or even more virulent to humans than the Classical BSE agent. While mankind has been in contact with the major TSE of small ruminants for centuries, there is no epidemiological evidence to suggest that classical scrapie is zoonotic; however, experimental transmission data on humanised mice and non-human primates have been very scarce so far.

What does this mean for the future? The decline of the BSE epidemic seen by 2005 led to consideration of some relaxation of costly BSE control measures as depicted in the EU TSE Roadmap (EC, 2005), and will inevitably be followed by further relaxation as already outlined in another EU TSE Roadmap 2 of 2010 (EC, 2010). It remains critical that current levels of consumer protection are maintained and all future changes from well established and highly effective current risk management measures are based upon sound scientific advice that EFSA will continue to provide.

Which old issues will remain, and which new issues will become relevant? For Atypical BSE, the most widely accepted hypothesis is that of a spontaneously arising (“sporadic”) disease in relatively old bovines. If this holds true, it will be impossible to eradicate such a disease which originates *de novo*; probably we then have to live forever with a ban on SRMs, in particular the central nervous system (CNS), of older cattle. Given our insufficient knowledge about the true prevalence of atypical animal prion strains in the field, it will be important to continue and improve the systematic surveillance of animal TSEs, and to refine our diagnostic and laboratory methods and experiments. As some scientific data suggest that there is probably no absolute molecular barrier to transmission of TSE agents between mammalian species (EFSA Panel on Biological Hazards (BIOHAZ) and ECDC, 2011), the issue of a zoonotic potential of prions is likely to remain with us a time. For human TSEs including sporadic CJD, it will be important to continue systematic surveillance that should be able, as clearly shown with vCJD in the past, eventually to identify emerging new phenotypes or new prion strains. In sum, at a time when many scientists and most decision makers are no longer interested in prions and their risk, it will be prudent to stay vigilant, although this must be in a way that is balanced with other risks to human and animal health. In the risk assessment area, this will continue to be a challenge for EFSA in the years to come.

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