

BSE: the big issues

John Pattison

The government inquiry to establish and review the history of the emergence and identification of BSE and new variant CJD in the UK ran through most of 1998. The report is due in June. SEAC has an important and difficult role in advising the government on all matters relating to TSEs. Here Sir John Pattison, current Chairman, gives a personal view of the major issues that have confronted SEAC over the past few years.

● The UK Spongiform Encephalopathy Advisory Committee (SEAC) was created in 1990. I did not join until January 1995, but in every one of the 36 meetings since then it has struck me that there have been one or two big issues to discuss. Although some issues are discussed over and over again, the prominence of others has changed over time. It is interesting and instructive to reflect on the nature of the big issues over the last 4 years.

● CJD in farm workers

The first meeting that I attended, on 13 January 1995, when David Tyrrell was the Chairman, was a special one convened to discuss the death of a dairy farm worker from suspected CJD. This was the third case of CJD in someone working with a herd of dairy cattle in which BSE had been confirmed. Later in the year (4 October 1995) another meeting was called to discuss the significance of a fourth case of CJD in a cattle farmer with BSE in his herd. The chances of finding, between 1990 and 1996, four cases of CJD in farmers who had BSE in their herds was calculated to be about 1 in 10,000. This was worrying but we noted that there was a similar incidence of CJD in farmers, including dairy farmers, in countries with no or very few cases of BSE and that the clinical and pathological details of the cases were the same as classical sporadic CJD. The committee emphasized the need for continued surveillance and for the inclusion of material from the farmers in the strain-typing studies in the Neuropathogenesis Unit at Edinburgh. Now, 4 years later, we know that these cases in farmers have the molecular and biological features of classical sporadic CJD.

● Transmission via bovine tissues

My first meeting as Chairman took place in November 1995. In the months prior to that meeting evidence had been accumulating that the level of compliance with the SBO (Specified Bovine Offals) regulations was unsatisfactory. It appeared that small pieces of spinal cord might be left in as many as 1 in 200 inspected carcasses and this was unacceptable. The SBO regulations had come into force initially in 1989 and they represented the main measure for the protection of public health. This was exactly the right public health measure to introduce and over the years the extent of the measure was repeatedly reinforced. This occurred when additional tissues (such as terminal ileum) were found to harbour the transmissible agent; we felt late in 1995 that we had to recommend a ban on the production of mechanically recovered meat from bovine vertebral column so as to ensure that no bovine spinal cord entered the human food chain; the inspections of compliance with the regulations were intensified from 1995 onwards; finally the sale of beef-on-the-bone was prohibited in 1997 when infectivity was found in the dorsal root ganglia.

● New variant CJD

The next big issue was new variant CJD (nvCJD). Slowly during 1995 and then rapidly at the beginning of 1996, confirmed and suspect cases of CJD in relatively young people were accumulating. At our meeting of 8 March 1996, Bob Will and James Ironside from the CJD Surveillance Unit reviewed the clinical and pathological details of eight cases. They were of the opinion that the young cases in the UK with their unique pathology and similar clinical features could be a new form of CJD. Members of the committee agreed with this and believed the findings supported the possibility of a new risk factor for CJD which might be exposure to BSE. Before coming to this conclusion though, we asked James to show the pathology to other neuropathologists and Bob to have further discussions with colleagues abroad to make sure that such cases had not been seen in other countries. We met a week later to confirm our conclusions and in the statement to ministers we included the sentence:

On current data and in the absence of any credible alternative the most likely explanation at present is that these cases are linked to exposure to BSE before the introduction of the SBO ban in 1989.

Much of the rest is well known and the big issues tended to be framed as questions. One question that was immediately asked was "Is there really a link between BSE and nvCJD?" The evidence for this was slow in coming because of the nature of the approaches to strain-typing. However, over the next 12–18 months it became clear that the molecular PrP^{Sc} type of nvCJD was different from other forms of CJD and indistinguishable from BSE and Feline SE (FSE). Moreover, the incubation period and lesion profile of infectivity from nvCJD cases in inbred strains of mice was once again different from sporadic CJD and the same as FSE and BSE.

● Transmission between species

The next question that was asked was "How was the disease transmitted to humans?" Our hypothesis has always been that it was likely to be exposure to bovine nervous system tissues in beef products prior to the specified bovine offals ban, but it is hard to gather evidence to support this. There is a pleasing unity about the concept that the cattle epidemic was fuelled by the ingestion of contaminated feed:



that this feed was also responsible for infecting exotic antelopes in zoos; that domestic cats were infected by the inclusion of bovine brain and spinal cord tissue in pet food; that wild cats in zoos were infected through eating carcasses of BSE-affected animals which contained spinal cord and that humans were also infected by the oral route. We think it likely that brain and spinal cord were included in the human food chain prior to the offals ban and that this is the most likely source of contaminated bovine tissue. Nevertheless, we regularly consider issues related to gelatin, tallow, milk, ox blood and the destination of various effluents from rendering plants. We also recognize that it is important not to concentrate our thinking entirely upon bovine tissues and this brings us inevitably to sheep. The Committee started thinking about this issue early in 1996, made a long statement later that year, another one in 1997 and again in July 1998. It was surprising to see the media reaction to the most recent statement, bearing in mind that nothing had changed over the last 2–2½ years. The issue is straightforward. Sheep can be infected experimentally by the oral route with less than 1 gram of BSE brain. Some sheep in the UK were fed significant amounts of MBM-containing feed and it would be surprising if some of them were not infected in the past. In the experimentally infected sheep the BSE agent can be recovered from the spleen in contrast to the situation in cattle. Thus BSE in sheep has at least one property different from BSE in cattle and similar to scrapie in sheep and it might therefore acquire other scrapie-like properties, one of which is to sustain the agent in the flock once it is there. Thus it is possible to sustain a theoretical argument that BSE might be present currently in some sheep in the UK. If you ask the question "Is there any evidence of this?", the answer is no. But, if you ask the question "Has the national flock been adequately surveyed for this?", then the answer is also no. So the only logical

thing to do is to conduct an expanded programme of research into scrapie, the disease and the nature of the strains causing current cases. It will take some time to accumulate the necessary data and in the meantime the UK and Europe are pursuing a risk reduction strategy by banning the easily accessible risky material from sheep, namely brain, spinal cord and spleen.

● The future

The third question that has been asked since March 1996 is "How many cases of nvCJD will there be?" Following the March 1996 announcement the answer to that question had to be a very broad range from no more cases than had already been observed, to a large six- or seven-figure number. To date there have been 3 patients who died of nvCJD in 1995, 10 in 1996, 10 in 1997 and 12 in 1998. The continuing uncertainty about the relative sensitivity of the human population, the patterns of exposure to BSE and the average incubation period of nvCJD means that a very wide range of total epidemic sizes is still compatible with the observed annual incidence to date. This therefore remains the biggest issue of all and one that will not be resolved quickly. The reason it is so important is that an ability to narrow the range and determine whether it is relatively high or low would be very helpful in many of the policy decisions that have to be taken. The emphasis is now shifting away from possible exposure of the UK population to BSE through beef products to the possibility of human-to-human transmission via medical or surgical procedures. As precautionary measures in the face of uncertainty some plasma products are derived from non-UK sources, leucodepletion of blood for transfusion is being introduced and the cleaning and sterilization of surgical instruments is under consideration.

1999 will be another important year in relation to BSE and related diseases. The epidemic in cattle is expected to continue to decline rapidly. However, big issues remain and it will be some years yet before we know the full consequences of BSE. In the middle of the year we will have the report of the Public Inquiry into BSE and we will have a judgement about whether or not we could have handled the issues better.

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LEFT: Computer model of a prion protein. COURTESY, JIM HOPE, INSTITUTE FOR ANIMAL HEALTH, COMPTON