

# Bovine spongiform encephalopathy (BSE) revisited

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## Summary

Since 2001, bovine spongiform encephalopathy (BSE) has continued to attract considerable scientific interest. It is now widely accepted that abnormal prions (proteinaceous infective agents) in bovine products can transmit BSE between cattle and are the cause of (new) variant Creutzfeldt–Jacob disease (vCJD) in humans. A better understanding of transmissible spongiform encephalopathies (TSEs) and how they propagate will affect how we feed and manage our livestock and prepare their products for entry into the human food chain; it should also advance our understanding and management of vCJD. This disease is invariably fatal although recently there have been reports of possible immunization using monoclonal antibodies or use of drugs to prevent infection or extend the quality of life of those infected. To date about 150 people have died of vCJD, mainly in Europe. Predictions of future deaths from vCJD have been revised downwards but are still uncertain. Countries outside the EU that have newly reported BSE cases include Israel, Japan and most recently Canada; it is probable that there are cases in other Asian countries that have not been detected. The case in Canada has again raised questions about the possibility of cross–species transmission (to humans or livestock) of TSEs such as chronic wasting disease (CWD), a widespread disease of farmed and feral deer and elk in Canada and the USA.

All evidence indicates that Australia is free of BSE, but we must remain proactive. Safeguards are in place that should prevent the entry of BSE infection. Veterinary oversight and contingency plans should maximize the chances of our quickly diagnosing and eliminating BSE from domestic cattle if, as seems unlikely, a case of BSE should be detected.

**Keywords:** mad cow disease, TSE, BSE, CJD, CWD, prion

## Background

Two years ago I reviewed the situation in Europe

and Australia concerning bovine spongiform encephalopathy (BSE, or ‘mad cow’ disease) and its human equivalent (variant Creutzfeldt–Jacob disease, vCJD). I outlined the nutritional issues thought to have contributed to the development of these diseases in Europe and considered the strategies then in place to minimise Australia’s risk of exposure to these diseases and their possible limitations (Nolan 2001). My conclusion then was that the risk of BSE transfer from overseas to domestic cattle in Australia was negligible. Provided we remain vigilant, this low risk should continue. My intention in this paper is draw attention to some of the newer scientific findings and to consider their implications.

## BSE transmission

The prevailing view is still that the infective agent is a particle of glycosylphosphatidylinositol–attached protein, or ‘prion’, which is concentrated in neurons and haemopoietic cells (Risitano *et al.* 2003). According to the protein–only hypothesis of prion propagation, an abnormal isoform (designated PrP(Sc)) of a normal cellular protein (PrP) accumulates in brain and lymphoreticular tissues. The abnormal prion is the principal or sole component of transmissible prions and in this regard prions are still a scientific curiosity in being able to replicate without the involvement of nucleic acids. When an animal is infected, the abnormal isoform is thought to trigger a chain reaction with normal prions in the cytosol causing them, by an unknown mechanism (Lucassen *et al.* 2003), to replicate the configuration of the infective prion. This infective protease–resistant isoform is extremely resistant to the traditional rendering processes used to make meat and bone meal (MBM). If infected MBM is fed to cattle, the infective prions may be absorbed by uninfected animals triggering their normal prions to convert to the abnormal isoform. Although the infective prions are concentrated in nerve and lymphoid tissues, other bovine products are potentially infective; for example, recently

tallow in milk substitutes has been reconsidered as a possible, though probably unlikely, route of infection in calves (see later). It is widely believed that the feeding of BSE-infected bovine products back to cattle created the ‘amplification cycle’ that sustained the BSE epidemic in Europe. There is also general acceptance that ingestion of BSE-infected bovine meat or meat products by people is the major route of infection for the human neuro-degenerative disease referred to as (new) variant Creutzfeldt–Jacob disease (vCJD). Although similar to the long known ‘sporadic’ or ‘classical’ CJD, vCJD appears to be a new and quite distinct disease that was first recognised in the UK in 1996 (Will 1998; Will *et al.* 2002; Armstrong *et al.* 2002). Prions causing vCJD can also potentially be spread from person to person by contaminated surgical instruments, blood transfusions, donated organs and vaccines as occurs with other forms of CJD.

Proponents of these mainstream views accept that there is no direct proof that the BSE epidemic in cattle is the reason for the appearance of vCJD in the UK. Such ‘proof’ is elusive because to test whether BSE prions can infect humans by intentionally infecting them would be ethically unjustifiable, but establishing causality according to Henle–Koch postulates is equally problematic for other diseases such as HIV–AIDS for which the causes are nevertheless generally acknowledged. In this connection, a challenging paper was published in the British Medical Journal (BMJ) in October 2001 entitled ‘New variant Creutzfeldt–Jacob disease: the epidemic that never was’ (Venters 2001). Venters claimed the indirect evidence for a causal link between BSE and vCJD (see Scott *et al.* 1999) was questionable; he argued the epidemiological evidence did not support the link and cases of infection did not fit characteristic patterns expected for a food-borne infection. Venters hypothesised that ‘vCJD’ might be an extremely rare but previously existing and misdiagnosed form of CJD that came to light as a result of the improved detection of all forms of CJD by the UK CJD Surveillance Unit. Some of the respondents in the BMJ commended Venters for reopening the argument but, from my reading of the comments, generally added little evidence in support of Venter’s alternative views.

Ironsides *et al.* (2002) responded to Venter’s paper in a letter to the Editor of the BMJ under the heading: ‘New Variant Creutzfeldt–Jacob disease: the critique that never was.’ They refuted the arguments put forward by Venters (2001) and concluded, on the basis of an ‘assessment of a range of clinical, pathological, epidemiological and laboratory based evidence’ that ‘there is now overwhelming evidence that BSE is the cause of vCJD’. The arguments for the mainstream view include:

- the temporal and geographical association between the vCJD and BSE diseases; and
- biological strain typing and molecular

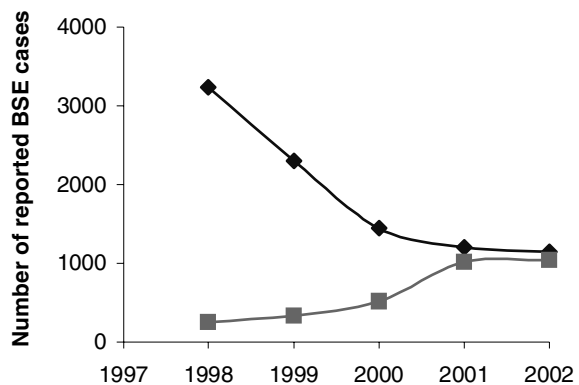
characterisation that indicate the same agent causes the two diseases.

Although it is widely held that transmission of BSE to humans is by ingestion of infected beef products, Concepcion and Padlan (2003) have reopened the question of alternative routes of infection by suggesting that scrapie in sheep or BSE in humans may be transmitted by faeces of prion-infected rodents. Their hypothesis is based on their noticing a close similarity between in the sequences of human and rodent prion protein in peptic digestion fragments that are in turn closely similar to the sequence of a prion known to be protease resistant and infective.

## The BSE epidemic

Reported cases of cattle deaths from bovine spongiform encephalopathy (BSE) in the UK have fallen over the last 5 years, but have tended to stabilize at about 1000 per year in 2001 and 2002 (Figure 1).

It is now 15 years since the first ban was placed on feeding bovine products to ruminants in the UK and about 7 years since the bans were actively policed. Thus, BSE infection should not exist in UK cattle less than 7 years old. It is not clear why cattle deaths from BSE have not continued to decline as rapidly in the last two years as in the previous three years. A low level of contamination of cattle feeds with infected meat or meat products may have continued after the 1996 ban. After the ‘over 30 months scheme’ (OTMS) for culling cattle was introduced, and 1.4 million UK cattle were slaughtered, potentially contaminated ‘specified bovine offals’ were stored in unused buildings (warehouses and aircraft hangers) pending incineration (Barnett 1999). The transport and handling of these materials may have permitted a low-level contamination of cattle feeds. Similarly, on-farm feed storage areas or feeding troughs previously used for feeding meat or bone meal to ruminants could have retained some residual infectivity and allowed carry-over of the infected agent into



**Figure 1** Numbers of reported cases of BSE in each of the last 5 years in the UK (◆) and in all other countries combined (■).

subsequently acquired feedstuffs. It is also possible that vertical transmission from cow to calf may have occasionally occurred.

Last year, the possibility was raised that milk substitutes used for feeding calves might have been a major and previously unsuspected route of infection in the early stages of the development of the BSE epidemic in the UK ([www.priondata.org](http://www.priondata.org)). Young calves are more able to absorb larger molecules, presumably including infective prions, than older cattle and would therefore be more susceptible to developing BSE after receiving relatively low doses of prions from the bovine tallow used in 'milk replacers'. Manufacturers in the UK claim they ceased using bovine tallow in milk substitutes in 1988 when the Government first banned the use of MBM for ruminant feeding, although their claim is now almost impossible to verify as samples do not exist. There also appear to be no data to indicate with confidence whether or not milk substitutes could convey prions. A retrospective analysis, however, suggests that BSE infection rates declined within one month of the government ban on use of MBM, and Dealler and Rainov (2003) have argued that this shows that more than 45% of animals developing BSE were being infected during the first month of life which is the period when they were likely to have been given milk substitutes. The argument that milk substitutes may have contributed to the spread of BSE in the UK is consistent with a higher relative incidence of BSE in the UK than in Northern Ireland where a higher proportion of cattle are beef animals.

Investigators of the BSE cases in Japan during the last three years believe the cows involved were given a milk substitute that probably contained tallow imported from the Netherlands where BSE was confirmed in 1997. The authors of two papers cited by Will (1999) listed 'protein impurities within the tallow' as possible sources of infection of the cattle reported to have developed BSE in Germany. In Japan, however, there was also the likelihood of MBM from the UK being used in calf feeding, as UK Customs records (HMCE 1988) show that considerable tonnages of MBM were exported to Japan up to the year 2000. On the other hand, Wilesmith *et al.* (1988) suggested that tallow was not a likely source of BSE transmission. The Scientific Steering Committee of the European Commission (EC-SSC 2003) concluded that 'with regard to BSE risk, cattle tallow is being classified in the lowest category of infectivity; the SSC has not classified it as "not infectious"'.

This month, Lupi (2003) has opened discussion of whether ectoparasites might be vectors for prion diseases, noting that iatrogenic transmission can occur via corneal transplants and animals can become infected via eye inoculation with infected brain tissue. Also several human-skin cell types are susceptible to infective prion proteins and several ectoparasites and adult flies can express prion proteins.

The EC Scientific Steering Committee has issued two opinion statements on the hypothesis suggesting

possible links between BSE and organophosphate (OP) that had been used in the UK in sheep dips and against warble fly infestation. EC-SSC (1988) and EC-SSC (2001) both concluded that there was no evidence in support of an OP origin of BSE. Earlier this year, additional enquiries on the issue were addressed to the EC. The Committee has recently concluded (EC-SSC 2003) that 'there is no additional information on the claimed involvement of OPs in the origin of BSE'.

While the reported cases of BSE in the UK in the last 5 years have declined, cases reported elsewhere have risen to about 1000 per year (Figure 1), Israel reported its first case of BSE in 2002. Seven cases have been reported to date in Japan, the most recent being in January 2003. Japan is the only Asian country to report BSE where there has been mandatory testing for BSE since 2001. Although the BSE agent may have reached domestic cattle in most Asian countries, surveillance and risk analysis for BSE contamination of imported products is not routine in 10 out of 16 countries (Ozawa 2003). Nevertheless, the likelihood of amplification of BSE to epidemic proportions in these countries is considered by Dahlanuddin *et al.* (2003) to be low because there is little routine use of MBM as a protein supplement for ruminants in these countries.

One new case of BSE was reported in Alberta, Canada in May 2003. This case has had major ramifications for Canada's US\$1.4 billion beef industry; the United States, Japan, Australia, South Korea, Singapore, New Zealand, Indonesia and Barbados have all banned beef imports from Canada indefinitely. At the time of writing (June 2003), 15 farms in Alberta, Saskatchewan and British Columbia are still under quarantine and 1,160 animals have been slaughtered and tested for BSE. All the tests have been negative. The Canadian Food Inspection Agency initiated DNA testing to determine where the BSE-infected cow was born with a view to limiting the number of animals needing to be killed and tested for BSE. The DNA testing has been inconclusive, and the birthplace of the infected animal and the source of the infection are still unknown. The source may never be found but Canada, like Japan, was one of the countries that records (Eurostat 2000) show continued to import MBM from the UK after MBM feeding in the UK was banned in 1988. The tracing of bulls from the same herd as the BSE infected cow to Montana also potentially includes the USA in the need for increased ongoing testing in both countries; current levels of surveillance would probably not detect cases of BSE in cattle in north America if they were at the levels currently still existing in the UK. The handling of the new case in Canada could have lessons for Australia, and an analysis of the Canadian response is currently being undertaken by the Department of Agriculture Fisheries and Forestry, Australia (AFFA).

The new case of BSE in Canada has renewed public speculation that chronic wasting disease (CWD), a spongiform encephalopathy of Cervids (elk and deer) that occurs in the USA and Canada might have been

passed to cattle. It has previously also been suggested that CWD might infect people. In contrast to BSE, CWD appears to be maintained within captive populations of deer and elk by salivary, urinary and faecal routes and, possibly, maternal transmission (Williams and Miller 2003). Attempts by Williams and colleagues at the University of Wyoming to infect cattle by holding them in close proximity to infected mule deer suggest that transmission does not occur under natural conditions, even though cross-infection is possible if the CWD infective agent is injected directly into the brain of cattle. The announcement (USGS 2003) for a CWD forum to be held this month in Madison comments: *The incidence of CWD in wild animals is of great concern. The disease was originally described in captive animals 35 years ago in Colorado. However, over the last five years, CWD has been found in wild herds in several surrounding states and Canada. In early 2002, CWD has been detected in wild deer in South Dakota, Wisconsin and New Mexico. Researchers speculate that CWD could have been transported long distance as a result of interstate shipment of infected animals.* In April this year, Williams and her colleagues were awarded a US\$2.4 million Department of Defense grant to develop methods for environmental testing for the presence of the CWD infective agent. To date, however, CWD has not been identified in Cervids in Alberta where the recent case of BSE occurred. In relation to possible CWD infection of humans, Belay *et al.* (2001) reported on three cases of CJD all in unusually young patients who had eaten game meat in the 1980s and had died after having progressive neurological symptoms. In April, the case reports of two patients at the Seattle VA hospital who had developed CJD and had been deer and elk hunters were reported at the 55<sup>th</sup> meeting of the American Academy of Neurology in Honolulu. The presenters (Murinova *et al.* 2003) noted that the neuropathological similarities of the two cases were striking and concluded they 'may represent a new entity in the spectrum of prion diseases'. In contrast, workers involved in the Colorado Surveillance Program for CWD transmission to humans reported on the deaths of two people with neurological disorders and a history of exposure to deer and elk. One had symptoms consistent with Alzheimers disease and the other with familial CJD. They emphasized the need for a 'thorough clinical and neuropathologic examination' before attributing any neurological disorder to CWD exposure. While there is at present no clear evidence that CWD is linked to any form of CJD, there clearly are concerns as the US government has issued warnings to people not to eat brain or lymphoid tissue and to use gloves when handling carcasses.

### vCJD cases

In the UK, 135 people have now (June 2003) died of vCJD and a further 6 people have been diagnosed with vCJD. Elsewhere in Europe there have been 9 cases

with another two possible cases now under investigation in Guadeloupe. Two cases have been diagnosed in Hong Kong and two in North America but all four were probably infected in Europe. In contrast to predictions being made two years ago, some researchers now consider the incidence of vCJD in the UK may already have peaked; numbers of deaths expected from vCJD have been revised from 7000, based on data collected until the end of 2001, to much lower numbers based on data to the end of 2002. Anderson *et al.* (1996) predict about 12 deaths in the next 12 months and researchers at Imperial College, London (Ghani *et al.* 2003a, 2003b) are predicting about 70 deaths during the next 5 years (range 10–200). There are two caveats. First, predictions refer only to people becoming infected as a result of eating BSE-contaminated meat and do not include iatrogenic infection, e.g. via infected surgical instruments or blood infusions. Second, all cases to date (the database for the current predictions) have been drawn from the 40% of people who are homozygous for methionine at codon 129 in the prion gene. Codon 129 can also code for valine but there is no evidence that vCJD has yet occurred in Britons who are MV or VV genotypes (Hillier *et al.* 2001). An optimistic consideration is that this 60% of people are not susceptible to vCJD. An alternative possibility is that, because polymorphisms in the prion gene are known to affect incubation times and TSE susceptibility in humans and mice (Collinge *et al.* 1991), BSE incubation periods in the MV or VV may be longer than in the MM genotypes. If so, it is still possible there are people who are 'silently' infected and will, in the future, contribute to a new wave of vCJD cases.

The first estimates of 'silent' vCJD cases, i.e. infected people without clinical symptoms, were published last year (Hilton and Ironside 2003). One positive sample was identified by an immunohistochemical technique among 8318 samples of lymphoreticular tissues (70 % appendix and 30 % tonsil) obtained during routine autopsy or surgery in people aged 10–50 between 1995 and 1999. The sample size was too small to be statistically helpful, giving an 'estimated detectable prevalence of prion protein accumulation of 120 per million' (95% confidence interval 0.5–900). A larger study is now being undertaken by John Collinge and co-workers, MRC Prion Unit, St Mary's Hospital, London. A problem for future studies on fresh material is that 50% of tonsillectomies are on children under 10 who are, and will progressively be, less likely to have been exposed to infection.

### Action of prions

Ma *et al.* (2002) and Ma and Lindquist (2002) have determined that whilst abnormal prion isoforms are the infectious agents, apparently they are not the agent that kills neurons. Newly produced normal prions locate in the cell membrane and are expressed on the surface of

the membrane. Abnormal prions are returned to the cytosol and are destroyed by proteosomes. In infected animals, normal isoforms are transformed to abnormal isoforms by a self-sustaining chain reaction, but the latter were not themselves toxic when injected into mice genetically altered so that they do not make prions. Instead the abnormal isoforms appeared to somehow overload the proteosomal disposal mechanism and accumulation of even small amounts of abnormal prions in the cytosol was highly cytotoxic. These workers have shown in mice that toxicity is exacerbated by proteosomal inhibitors.

### Transmission of the infective agent through the body

Recent studies suggest that B lymphocytes or prion-protein expressing B-cell dependent follicular dendritic cells may carry infections from peripheral sites of entry (Brown *et al.* 1999); however, infection has also been established in mice that are deficient in B-cells (Schlomchik *et al.* 2001). Baker *et al.* (2002) have noted that neurons are often assumed to be the main site of replication of the infectious agents causing CJD, scrapie and BSE because the abnormal prion isoform amyloid accumulates there, but their studies indicate that microglia, cells of myeloid origin with migratory activities in the brain, can have similar infectivity to brain homogenates whilst containing far fewer prions. They have pointed out that microglia are often considered to have a secondary reactive role in CJD, responding to brain injury and infections by alterations in morphology, gene expression and cytokine release (Zielasek and Hartung 1996). On the other hand, they can also develop macrophage or dendritic cell properties and peripheral myeloid cells can harbour the CJD prion for at least 5 weeks in vitro (Manuelidis *et al.* 2000). Baker *et al.* (2002) used reverse transcription polymerase chain reaction analysis to demonstrate that CJD-infected microglia from mice show differences in morphology that are indicative of activation by infection, as well as inflammatory and immune responses. They concluded that migration of infected microglia through the brain parenchyma could enable CJD to enter and leave the brain before the appearance of pathological changes in the neurons.

Baker and Manuelidis (2003) analysed RNA from microglia with relevant cDNA arrays and identified about 30 transcripts not previously examined for any TSE. The expression profiles for CJD-infected microglia differed from those of microglia stimulated by experimental inflammatory agents such as lipopolysaccharide suggesting that the profiles might be helpful in diagnosis of infected microglia.

### BSE contaminated products

Studies have shown that captive bolt guns used to stun animals could spread potentially infective material

through the blood and other tissues of cattle at the time of slaughter. Anil *et al.* (2001) found brain particles in the jugular blood from four out of 15 cattle stunned with one type of gun that uses a blast of air to clean the bolt while still in the animal's heads. A second method of testing for dissemination of brain particles involved testing carcasses for contamination with nervous tissue that is normally found only in the brain and contamination was found at various sites in the body (Love *et al.* 2000). A third method was to introduce an easily detected marker bacterium (*Pseudomonas fluorescens*) into the captive bolt site or with the bolt itself. The bacterium was found in muscle, blood and other organs in the carcass but also on the hands of the worker operating the gun and in the environment where the gun was used (Daly *et al.* 2002). In January 2002, the Scientific Steering Committee at the EC accepted that captive bolt guns could cause dissemination of brain particles through the carcass and wanted more research to be undertaken urgently. However, they also concluded the use of non-penetrating stunners or electronarcosis present a negligible risk of brain particle dissemination.

### Diagnosis of TSEs

Definitive diagnosis of TSEs relies mainly on post-mortem detection of abnormal prion isoforms in the brain. Ante-mortem tests currently in use and those showing promise were reviewed at a Regional Workshop on BSE Diagnosis and Surveillance held in Thailand (OIE/FAO-APHC 2002). One test marketed by Prionics AG Ltd (Switzerland) relies on use of Western Blot. Enfer (Ireland) have developed ELISA or immuno-histochemistry tests using a monoclonal antibody derived from PrP-null mice immunized with a recombinant bovine prion sequence; the antibody binds to an epitope within the core of the abnormal prion isoform and the method has specificity for cattle, pig and humans. Other antibodies have been raised to different parts of the bovine prion sequence. These tests are marketed commercially and have been validated for rapid diagnosis by scientific committees of the EU. Boehringer/Ingelheim have been working on a test that should detect BSE in blood samples from cattle during the incubation phase. Methods are also under development for detecting prion fragments that, despite being below levels of detection in blood, are sufficiently concentrated in urine to be detectable by immunological methods (Shaked *et al.* 2001).

### Treatments for vCJD

There are as yet no effective treatments for vCJD in infected people. Some researchers are attempting to develop vaccines. Burton *et al.* (2001) identified a mouse antibody that blocked prion infectivity in cells in tissue culture. Researchers at the New York University School of Medicine (Wolf 1996) demonstrated that a

bacterial recombinant mouse prion caused an immune response in mice that delayed the onset of a TSE. Although this work could lead to vaccines against TSEs in sheep and cattle, these workers have warned that the vaccine might cause an autoimmune disease and, while the risk might be acceptable in farm animals, it would preclude use of the vaccine for delaying the onset of CJD in people.

Recently legal permission was granted to the parents of a Northern Ireland teenager, Jonathan Simms for the use of an experimental drug, pentosan polysulphate, to treat vCJD. The patient is said to have 'improved' after being given 12 injections of increasing doses of pentosan polysulphate directly into the brain. Pentosans have been shown to inhibit accumulation of abnormal isoforms of scrapie prion in mice neuroblastoma cell lines (Prince *et al.* 2003) and UK researchers found it extended the incubation period for the disease (Dealler and Rainov 2003). The mode of action is unclear but pentosan polysulphate may reduce the activity of interleukins involved in the inflammatory response or prevent the conversion of normal prions to the abnormal isoform. Recently, White *et al.* (2003) reported that monoclonal antibodies against the normal prion but with little affinity for the abnormal prion isoform can prevent the conversion *in vitro* of normal prions into the infective isoforms, and prion-infected mice treated with these antibodies remained healthy for over 300 days after untreated animals infected at the same time had died. In the USA, Sigurdsson *et al.* (2003) have also shown that immunisation of mice with anti-PrP<sup>c</sup> antibodies following their exposure to infective prions increased the period of incubation of disease.

Schmitt *et al.* (2002) have developed a simple and inexpensive test using blood serum that reliably detects scrapie in hamsters and should be extendable to other TSEs including vCJD. The method uses an infrared (FT-IR) spectroscopy-based approach and optimised artificial neural networks (ANNs) and can detect characteristic molecular alterations in the serum of infected animals. Optimized ANNs consistently yielded test sensitivities and specificities of 97% and 100%, respectively. The predictive value of a positive (negative) test was 100% (98%).

## Australia

Australia is still one of about 18 countries judged by the European Commission to meet 'Category 1' BSE status. This status is currently undergoing a routine reassessment by the EC and the Organisation Internationale Epizootie, Paris (OIE). Three key measures are in place in Australia to maintain this rating which is imperative if Australia is to maintain market access with trading partners, and domestic and overseas consumer confidence in the safety of our beef products:

- strict controls and restrictions on imports of live animals, genetic material and animal feedstuffs: importation of MBM and similar products was banned in the mid 1960s from all countries except New Zealand;
- a ban on feeding meat and bone meal (MBM) to ruminant animals, and audits on compliance with feed bans;
- a national surveillance program (surveillance was begun in 1990 and a national TSE surveillance program was established in 1998).

In brief, Australia banned importation of stock feeds of animal origin in 1966. Importation of all live cattle from the UK and Ireland was banned in 1988 and extended to include France and Switzerland in 1991.

Australia banned importation of specified foods containing British beef and beef products in 1996, the year the probable link between BSE and vCJD was announced in the UK, and the livestock industries adopted a voluntary ban on the feeding of ruminant-derived MBM to ruminants that became law in 1997.

## Contingency plans and action by authorities

Australian authorities have responded quickly to recent BSE outbreaks overseas. After the first case of BSE was reported in Japan in September 2001, Australia suspended the importation of all beef and beef products from Japan, and the Australian and New Zealand Food Authority (ANZFA), now Food Standards Australia and New Zealand (FSANZ), asked Australian retailers to withdraw Japanese beef products. When the new case of BSE was reported in Canada in May 2003, Australia immediately banned beef imports from Canada for an indefinite period, pending further investigation. At the time of writing, Brazil, New Zealand, Norway, Sweden, United States and Vanuatu as well as Australia were accorded Category A status by FSANZ. Canada was given the lower status of other countries with confirmed cases of BSE but the status of the US is still rated as Category A.

The Australian Veterinary Emergency Plan (AUSVETPLAN) contains emergency response procedures and guidance for events relating to entry of exotic diseases. Animal Health Australia, the custodian of that plan works closely with the Commonwealth, states and territories and the livestock industries at a district level to determine priorities and regularly update its manual which is available in print and on line. Version 3.0 (AUSVETPLAN 2003) contains the latest version of the plans for an incursion of BSE.

The available evidence indicates that domestic cattle in Australia are currently BSE-free and likely to remain so. Nevertheless, it is quite probable that cases of the human equivalent of BSE, vCJD will be

discovered in Australia as Australians have travelled extensively and some will have ingested beef in Europe in the period of the BSE epidemic. A document entitled 'How Australia will respond to our first case of vCJD: A guide to the Public' has been made available at the websites of the National Health and Medical Research Council (NHMRC) ([www.nhmrc.gov.au](http://www.nhmrc.gov.au)) and the Commonwealth Department of Health and Ageing ([www.health.gov.au](http://www.health.gov.au)).

Some questions as to whether import restrictions might still be further 'fine tuned' to ensure Australia's BSE-free status were raised at our previous biennial meeting (Nolan 2001). A recommendation was made then for on-going consideration of whether feeding of animal proteins to non-ruminant livestock (pigs, chickens and perhaps fish) should be banned as has occurred in EU countries. This issue is again emphasized by the BSE case in Canada (and cases in Japan) that may have arisen from feeds contaminated with BSE that have been entering both countries until quite recently (Eurostat 2000). In Australia, the risks of feeding MBM to non-ruminants is low because we do not have BSE or scrapie in farmed or non-farmed animals, and we have not imported MBM since 1966. I. Parsonson and D.B. Adams (Agriculture Fisheries and Food Australia) are currently assessing the risks of this practice for the NHMRC Special Expert Committee on the TSEs (SECTSE) and will probably recommend that the practice should be allowed to continue.

Some other issues deserving of further consideration that were raised in 2001. Some of these have been covered by the changes made since then, for others the situation is under review but no changes have been considered to be warranted. For example, current information suggests that semen and embryos can be safely imported, but this issue remains under review. In October 2002, SECTSE reviewed the risks associated with imported vaccines and endorsed the policy statement from the Commonwealth's Chief Medical Officer indicating that the risk of contracting vCJD via vaccines is extremely low; but SECTSE also endorsed the Therapeutic Goods Administration's intention, in the future, to source vaccines from processes that do not use foetal calf serum.

### Risks with imported foods

In relation to the risk of importation of BSE-infected foods, ANZFA commissioned a BSE risk assessment by 10 overseas scientists who were due to report their findings in October 2001. There is apparently no published report of those investigations.

In September 2001, FSANZ introduced a new certification system within which the food standards code was amended to require that all 'bovine meat and food ingredients derived from bovines must be derived from animals (deemed) free from BSE'. These measures replaced a provisional suspension of importation of beef and beef products from 30 countries introduced in

January 2001. This 'BSE-free' certification requirement is still in place: it relies partly on the exporting country's claim that it has taken all steps necessary to ensure that its cattle are BSE-free, but also on ANZFA's assessment of risk based on its classification within four categories moving from Category A ('negligible risk') to Category D ('highest risk'; no imports allowed).

At about the same time, ANZFA also announced it would undertake a review of country of origin labelling with the comment that this issue 'is also more complex and contentious than it might initially appear to be'. Again, perhaps for this reason, ANZFA does not appear to have released any further public information on this important matter.

On the basis of scientific evidence in 2001, FSANZ had concluded that the BSE risk from milk and dairy products, gelatine, fats and tallow, collagen from bovine skins and hides, and non-beef flavourings did not justify any import restrictions for these products (ANZFA, 2001). Since then, and after a comprehensive scientific risk assessment, the Code has been amended to allow importation of bulk tallow and bone-derived gelatine only if derived from cattle in countries that are deemed BSE-free.

In December, 2002 the Australia New Zealand Food Standards Code became the single Code for both countries.

### Epilogue

Despite the 'best laid plans', 'accidents' that could undermine our BSE security still happen. In October 2001, the Managing Director of ANZFA, I. Lindenmayer commented (ANZFA 2001):

*I was very disappointed when French corned beef re-appeared in some discount stores in Tasmania causing ANZFA to take immediate action together with the Tasmanian Department of Health and Human Services to have it removed from the shelves. Reportedly, the product had been landed in Australia prior to the introduction of wider restrictions on beef products in January 2001. This occurrence was rare as importers, distributors and retailers had responded quickly and responsibly to our request in January to remove European beef products from sale.*

A similar breach of regulations occurred in the UK in 2002 when bovine collagen was detected in Dutch chicken-breast fillets entering the UK from Europe. Species-specific DNA tests undertaken by the Irish Food Safety Authority indicated that the chicken contained bovine proteins. This event exposed a theoretical risk of BSE contamination to people in the UK eating the chicken, especially if the contaminating bovine protein was not produced and handled according to EU regulations.

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