Is the New Variant of Creutzfeldt-Jakob Disease from Mad Cows?

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A decade ago, the first instances of "mad cow disease" [bovine spongiform encephalopathy (BSE)] were described in what has become a major epidemic of more than 160,000 cases in cattle in the United Kingdom (UK) (see figure). Recently, BSE has been linked to 10 cases of a new variant of Creutzfeldt-Jakob disease (CJD) (*1*), a severe neurologic disease of humans. This association has had major repercussions on Britain's relations with her European neighbors, has led to a ban on the export of British beef and a ban in the UK on the consumption of British cattle more than 30 months of age, and is likely to lead to large-scale culling of cattle to curtail the epidemic.

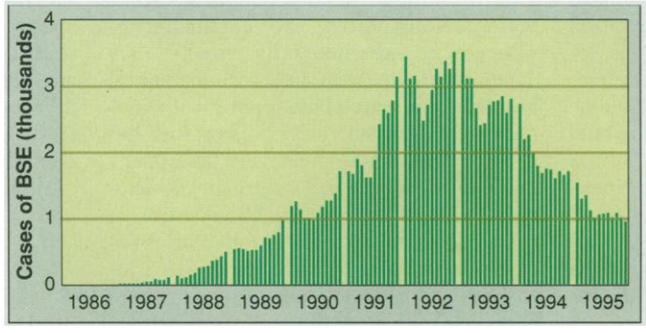
Both BSE and CJD are transmissible spongiform encephalopathies (TSEs), a group of diseases that includes scrapie (a disease of sheep) and kuru (found in humans). These diseases usually have an incubation period of years, and the agents that cause them are remarkable. The infectious agents are extremely resistant to inactivation and may contain no nucleic acid, being perhaps a normal host protein that has been posttranslationally altered. Cases of disease occur that may be genetic in origin but that are also transmissible (*2*).

Epidemiological studies linked early occurrences of BSE to the feeding of meat and bone meal (MBM) to cattle. This practice was not new, but the onset of infection appeared to coincide with the cessation of the use of solvent to assist fat extraction in the rendering process, used to produce MBM from offal, some of which was from sheep and cattle. Removal of the solvent-extraction step is thought to have reduced the sterilizing capacity of the rendering process, allowing the infectious scrapie agent to pass into MBM. Another possibility is that BSE was endemic in cattle, but rare and unnoticed, and the changes in the rendering process allowed the agent to be recycled to many more cattle (*3*).

The feeding of MBM to ruminants was banned in 1989, and BSE declined in cattle born subsequently, but more slowly than expected. This slower rate of decline has been attributed to "leakage" to cattle of MBM intended for nonruminants. In order to tighten controls, specified bovine offals were banned in pig and poultry feed in 1990, and now MBM is banned from all animal feed. Vertical transmission from mother to calf cannot be excluded, although such transmission alone could not maintain infection in the cattle population (*4*).

Instances of TSE in exotic animals in captivity have been linked to the consumption of MBM, and instances in domestic cats in the UK are assumed to be due to BSE-infected offal in cat food. The small numbers of cattle with BSE that have been reported outside the UK have generally been in animals exported from the UK or that may have consumed UK MBM (*4*).

In the 1960s, kuru, an epidemic TSE of humans in Papua New Guinea, was linked to exposure to infected human tissues during ritual funeral practices. Subsequently, evidence of a link between CJD in humans and sheep scrapie was sought but not found. This lack of a connection was the main basis for assuming that BSE would be most unlikely to have any implications for human health (*5*). Nonetheless, from 1989, cattle with BSE were removed from the human food chain, as were specified bovine offals, including those shown to be infectious in animal experiments (brain and spinal cord), from all cattle aged 6 months or older at slaughter.



The epidemic. Confirmed UK cases of BSE in cattle by month of onset.

Concern that BSE may have infected humans was triggered by recognition, in early 1996, of a new neuropathological variant of CJD affecting, with disease onset since 1994, 10 persons in the UK under the age of 45 years, an age group in which CJD had been rarely described (*1*). The possibility of a causal link between these cases and BSE was based on the temporal and geographical association in the absence of any other plausible explanation, assuming an incubation period of 5 to 10 years. It remains unclear why the new variant of CJD has been seen only in young adults.

When the scrapie agent is injected intracerebrally into laboratory mice, different strains of the agent are associated with characteristic incubation periods and neuropathology. Multiple strains of scrapie have been described. To date, BSE-infected material put into the same mouse systems has shown evidence of only one strain, and the same strain characteristics have been found in the TSE-infected domestic cats and zoo animals (*6*). These results provide strong evidence that the TSEs in these other animals are caused by exposure to BSE. Results of testing brain tissue from the human cases of the new variant of CJD in the mouse system are unlikely to be available until 1997, but these studies may provide the firmest evidence that the cases are due to BSE. If the new variant of CJD is truly caused by BSE, the number of cases may increase substantially in the next year. Surveillance for CJD has been heightened in the UK and elsewhere. Since the 10 cases were reported in March, only one more case has been reported in the UK and one in France, a major export market for British cattle.

That the new variant of the disease is due to BSE is plausible but unproven, and the magnitude of any risk to the human population is unclear. Measures were taken in the late 1980s to remove from the human food chain tissues that were most likely to be infectious, and if the recently described CJD cases are due to BSE, they probably relate to exposure in the 1980s. If the number of cases does not increase greatly, fears about the safety of British beef presently being sold may be unfounded. If the epidemic reaches large proportions, the measures being forced upon the UK government to eliminate BSE rapidly would be wholly justified on public health grounds. The UK government is injecting substantial new funds for research on the TSEs, but unless tests are developed for subclinical infection with the BSE agent, the most informative epidemiological data may only appear with time.

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