New variant Creutzfeldt-Jakob disease and bovine spongiform encephalopathy

**Background**

Variant CJD (vCJD) is a rare, degenerative, fatal brain disorder in humans. Although experience with this new disease is limited, evidence to date indicates that there has never been a case of vCJD transmitted through direct contact of one person with another. However, a case of probable transmission of vCJD through transfusion of blood components from an asymptomatic donor who subsequently developed the disease has been reported.

Since variant CJD was first reported in 1996, a total of 217 patients with this disease from 11 countries have been identified. As of October 2009, variant CJD cases have been reported from the following countries: 170 from the United Kingdom, 25 from France, 5 from Spain, 4 from Ireland, 3 from the United States, 2 in Portugal, 2 in Italy, and one each from Canada, Japan, and Saudi Arabia. Two of the three U.S. cases, two of the four cases from Ireland and the single cases from Canada and Japan were likely exposed to the BSE agent while residing in the United Kingdom. One of the 25 French cases may also have been infected in the United Kingdom. There has never been a case of vCJD that did not have a history of exposure within a country where the cattle disease, BSE, was occurring.

It is believed that the persons who have developed vCJD became infected through their consumption of cattle products contaminated with the agent of BSE or in three cases, each reported from the United Kingdom, through receipt of blood from an asymptomatic, infected donor. There is no known treatment of vCJD and it is invariably fatal.

**vCJD differs from classic CJD**

This variant form of CJD should not be confused with the classic form of CJD that is endemic throughout the world, including the United States. There are several important differences between these two forms of the disease. The median age at death of patients with classic CJD in the United States, for example, is 68 years, and very few cases occur in persons under 30 years of age. In contrast, the median age at death of patients with vCJD in the United Kingdom is 28 years.

vCJD can be confirmed only through examination of brain tissue obtained by biopsy or at autopsy, but a "probable case" of vCJD can be diagnosed on the basis of clinical criteria developed in the United Kingdom.

The incubation period for vCJD is unknown because it is a new disease. However, it is likely that ultimately this incubation period will be measured in terms of many years or decades. In other words, whenever a person develops vCJD from consuming a BSE-contaminated product, he or she likely would have consumed that product many years or a decade or more earlier.

In contrast to classic CJD, vCJD in the United Kingdom predominantly affects younger people, has atypical clinical features, with prominent psychiatric or sensory symptoms at the time of clinical presentation and delayed onset of neurologic abnormalities, including ataxia within weeks or months, dementia and myoclonus late in the illness, a duration of illness of at least 6 months, and a diffusely abnormal non-diagnostic electroencephalogram.

The BSE epidemic in the United Kingdom reached its peak incidence in January 1993 at almost 1,000 new cases per week. The outbreak may have resulted from the feeding of scrapie-containing sheep meat-and-bone meal to cattle. There is strong evidence and general agreement that the outbreak was amplified by feeding rendered bovine meat-and-bone meal to young calves.

**US surveillance for CJD**

The possibility that BSE can spread to humans has focused increased attention on the desirability of enhancing national surveillance for Creutzfeldt-Jakob disease (CJD) in the United States in order to detect variant CJD. Improving
methods to detect classic CJD, such as increasing the number of autopsies on patients with suspected prion disease, enhances the ability to identify cases of variant CJD.

The Centers for Disease Control and Prevention (CDC) monitors the trends and current incidence of classic CJD in the United States through several surveillance mechanisms. The oldest and most systematic method includes analyzing death certificate information from U.S. multiple cause-of-death data, compiled by the National Center for Health Statistics, CDC. During 1979-2003 the average annual age adjusted death rates of classic CJD have remained relatively stable. Moreover, deaths from non-iatrogenic CJD in persons aged <30 years in the United States remain extremely rare (<5 cases per 1 billion per year). In contrast, in the United Kingdom, over half of the patients who died with vCJD were in this young age group.

In addition, CDC collects, reviews and when indicated, actively investigates reports by health care personnel or institutions of possible iatrogenic CJD and variant CJD cases. Finally and very importantly,, in 1996-97, CDC established, in collaboration with the American Association of Neuropathologists, the National Prion Disease Pathology Surveillance Center at Case Western Reserve University, which performs special diagnostic tests for prion diseases, including post-mortem tests that can detect vCJD.

Prevention measures against BSE spread
To prevent BSE from entering the United States, severe restrictions were placed on the importation of live ruminants, such as cattle, sheep, and goats, and certain ruminant products from countries where BSE was known to exist. These restrictions were later extended to include importation of ruminants and certain ruminant products from all European countries.

Because the use of ruminant tissue in ruminant feed was probably a necessary factor responsible for the BSE outbreak in the United Kingdom and because of the current evidence for possible transmission of BSE to humans, the U.S. Food and Drug Administration instituted a ruminant feed ban in June 1997 that became fully effective as of October 1997. As of October 26, 2009, a regulation issued by FDA in April 2009 came into effect establishing an enhanced BSE-related feed ban in the U.S. This enhanced feed ban will further harmonize BSE feed control measures in the U.S. with those in Canada (see below). In addition, FDA continues to enforce its important 1997 mammalian-to-ruminant feed ban through its BSE inspection and BSE feed testing programs.

As of July 12, 2007, an enhanced BSE-related feed ban came into effect in Canada. CFIA established this ban to more effectively prevent and quickly eliminate BSE from Canada. The enhanced ban prohibits most proteins, including potentially BSE infectious tissues known as “specified risk materials” (SRM) from all animal feeds, pet foods, and fertilizers, not just from cattle feed as required by the ban instituted in 1997. The 1997 feed ban in Canada was similar to the feed ban instituted in the United States that same year. As recently reported by CFIA, removing SRM from the entire animal feed system addresses risks associated with the potential contamination of cattle feed during production, distribution, storage, and use. Applying the same measure to pet food and fertilizer materials addresses the possible exposure of cattle and other susceptible animals to these products. With this ban in place, CFIA expects BSE should be eliminated from the Canadian cattle herd by about the year 2017.

In late 2001, the Harvard Center for Risk Assessment study of various scenarios involving BSE in the U.S. concluded that the FDA ruminant feed rule provides a major defense against this disease.

Questions and answers regarding bovine spongiform encephalopathy (BSE) and Creutzfeldt-Jakob disease (CJD)

What is bovine spongiform encephalopathy (BSE)?
Bovine spongiform encephalopathy (BSE) is a progressive neurological disorder of cattle that results from infection by an unconventional transmissible agent.

More than 184,000 cases of BSE were confirmed in the United Kingdom alone in more than 35,000 herds.

The BSE epidemic in the United Kingdom peaked in January 1993 at almost 1,000 new cases per week. The outbreak may have resulted from the feeding of scrapie-containing sheep meat-and-bone meal to cattle. There is strong evidence and general agreement that the outbreak was amplified by feeding rendered bovine meat-and-bone meal to young calves.

The nature of the transmissible agent is unknown. Currently, the most accepted theory is that the agent is a modified
form of a normal cell surface component known as prion protein. The pathogenic form of the protein is both less soluble and more resistant to enzyme degradation than the normal form.

**Is BSE occurring in the United States?**

Yes, the first known case of BSE in the United States was identified in December 2003. On December 23, 2003, the U.S. Department of Agriculture (USDA) announced a presumptive diagnosis of BSE in an adult Holstein cow from Washington State. This diagnosis was confirmed by an international reference laboratory in Weybridge, England, on December 25. Preliminary trace-back based on an ear-tag identification number suggested that the BSE-infected cow was imported into the United States from Canada in August 2001. The preliminary trace-back identification of the animal was later confirmed by genetic testing.

On June 24, 2005, the U.S. Department of Agriculture announced receipt of final results from The Veterinary Laboratories Agency in Weybridge, England, confirming BSE in a cow that had conflicting test results in 2004. This cow was from Texas and represented the first endemic case of BSE in the United States.

On March 13, 2006, the U.S. Department of Agriculture (USDA) announced the confirmation of bovine spongiform encephalopathy (BSE) in a cow in Alabama. The newly confirmed case was identified in a non-ambulatory (downer) cow on a farm in Alabama. The animal was euthanized by a local veterinarian and buried on the farm. The age of the cow was estimated by examination of the dentition as 10-years-old. It had no ear tags or distinctive marks; the herd of origin could not be identified despite an intense investigation.

**Is BSE a foodborne hazard in the United States?**

Strong evidence indicates that BSE has been transmitted to humans primarily in the United Kingdom, causing a variant form of Creutzfeldt-Jakob disease (vCJD). In the United Kingdom, where over 1 million cattle may have been infected with BSE, a substantial species barrier appears to protect humans from widespread illness. Since variant CJD was first reported in 1996, a total of 195 patients with this disease from 11 countries have been identified. As of August 11, 2006, variant CJD cases have been reported from the following countries: 162 from the United Kingdom, 20 from France, 4 from Ireland, 2 from the United States (including the current case), and one each from Canada, Italy, Japan, Netherlands, Portugal, Saudi Arabia, and Spain. Similar to the two U.S. cases, two of the four cases from Ireland and the single cases from Canada and Japan were likely exposed to the BSE agent while residing in the United Kingdom. One of the 20 French cases may also have been infected in the United Kingdom. The risk to human health from BSE in the United States is extremely low.

**What is the variant form of CJD that the experts in the United Kingdom believe might be related to the BSE outbreak in cattle?**

In contrast to the classic form of CJD, the variant form in the United Kingdom predominantly affects younger persons (median age at death around 29 years) and has atypical clinical features. These atypical features include prominent psychiatric or sensory symptoms at the time of clinical presentation or early in the course of the illness, delayed onset of neurologic abnormalities, duration of illness of at least 6 months, and a diffusely abnormal non-diagnostic electroencephalogram.

The characteristic neuropathologic profile of variant CJD includes, in both the cerebellum and cerebrum, numerous kuru-type amyloid plaques surrounded by vacuoles and prion protein (PrP) accumulation at high concentration indicated by immunohistochemical analysis.

Recently published data indicate that the epidemic of variant CJD in the United Kingdom may have already reached a peak. A listing of monthly updated numbers of CJD and variant CJD cases in the United Kingdom is available at: https://www.cjd.ed.ac.uk.

**Is there evidence directly linking this newly recognized variant of CJD to BSE exposure?**

There is strong epidemiologic and laboratory evidence for a causal association between variant CJD and BSE. The absence of confirmed cases of variant CJD in other geographic areas free of BSE supports a causal association.

In addition, the interval between the most likely period for the initial extended exposure of the population to potentially BSE-contaminated food (1984-1986) and onset of initial variant CJD cases (1994-1996) is consistent with known incubation periods for CJD.

An experimental study reported in June 1996 showed that three cynomologus macaque monkeys inoculated with brain
tissue obtained from cattle with BSE had clinical and neuropathological features strikingly similar to those of variant CJD (Nature 1996;381:743-4).

A study published in 1996 indicated that a Western blot analysis of infecting prions obtained from 10 variant CJD patients and BSE-infected animals had similar molecular characteristics that were distinct from prions obtained from patients with other types of CJD (Nature 1996;383:685-90).

An experimental study involving inoculation of a panel of inbred mice with the agents causing BSE and variant CJD substantially increased the strength of the scientific evidence for a causal association between variant CJD and BSE (Nature 1997;389:498-501). In this study, groups of inbred mice and a group of cross-bred mice inoculated with brain homogenates from variant CJD cases were reported to have had latency periods and lesion profiles consistent with the BSE pattern.

The latency period, neuropathology, and disease-causing PrP isoforms in transgenic mice expressing bovine PrP that were inoculated with variant CJD, BSE, and scrapie brain extracts provided additional evidence supporting the link between BSE and variant CJD (Proc Natl Acad Sci 1999;96:15137-42).

Has CDC initiated increased surveillance efforts to determine whether the newly recognized variant of CJD occurs in the United States?
Yes. The possibility that BSE can spread to humans has focused increased attention on the desirability of enhancing national surveillance for Creutzfeldt-Jakob disease (CJD) in the United States.

The Centers for Disease Control and Prevention (CDC) monitors the trends and current incidence of CJD in the United States using several surveillance mechanisms. On a routine basis, CDC reviews the national multiple cause-of-death data taken from death certificates and compiled by the National Center for Health Statistics, CDC. In addition, with the support of the Council of State and Territorial Epidemiologists, CDC conducts follow-up review of clinical and neuropathology records of CJD decedents aged <55 years who are identified through the national mortality data analysis or reported by health care workers. This is the age group in which almost all of the vCJD cases worldwide have occurred to date.

In 1996-97, CDC established, in collaboration with the American Association of Neuropathologists, the National Prion Disease Pathology Surveillance Center at Case Western Reserve University, which performs special state-of-the-art diagnostic tests for prion diseases, including post-mortem tests for vCJD. These tests are provided free of charge to all U.S. physicians. For more information about the center, visit its website at: https://www.cjdsurveillance.com.

Currently, CDC works with selected state health departments on various enhanced CJD surveillance projects and education programs regarding the importance of autopsy to both the surveillance and diagnosis of CJD. In addition, CDC collects, reviews and when indicated, actively investigates specific reports by health care personnel or institutions in all states of possible iatrogenic CJD and variant CJD cases.

These surveillance methods for CJD enhance the ability to identify cases of variant CJD when such cases occur in the United States.

For more information about surveillance and diagnosis of CJD, see the following article: Creutzfeldt-Jakob Disease surveillance and diagnosis. Belay ED, Holman RC, Schonberger LB. CID September 15 2005;41:834-836.

A summary of the analysis of multiple cause-of-death data was published in the Journal of the American Medical Association on November 8, 2000 (Volume 284, No. 18, pp. 2322-3) and in Clinics of Laboratory Medicine in December 2002 (Volume 22, pp. 849-62).

Is BSE a foodborne hazard for travelers to Europe?
The current risk for infection with the BSE agent among travelers to Europe is extremely small, if it exists at all.

This information was developed by the Centers for Disease Control and Prevention.


Centers for Disease Control and Prevention, National Center for Infectious Diseases. Questions and Answers Regarding