

CJD, BSE, nvCJD Information

Creutzfeldt-Jakob Disease Bovine Spongiform Encephalopathy New variant Creutzfeldt-Jakob Disease

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An information resource produced by National Cattlemen's Beef Association, reviewed by a scientific panel of experts in the fields of veterinary medicine, prion/protein studies, neuropathology, and disease surveillance.

Scientific Panel and Experts

Veterinary Medicine

Linda A. Detwiler, DVM
Sr. Staff Veterinarian
USDA, APHIS, Veterinary Services
320 Corporate Blvd.
Robbinsville, NJ 08691

William D. Hueston, DVM, PhD
University of Minnesota
Center for Animal Health and Food Safety
1365 Gortner Ave.
St. Paul, MN 55108

Prion/Protein Studies

Rick Race, DVM
National Institute of Allergy and Infectious Diseases
Rocky Mountain Laboratories
P.O. Box 250
Corvallis, Montana 59828

Neuropathology

Pierluigi Gambetti, M.D.
Case Western Reserve University Institute of Pathology
2085 Adelbert Road
Cleveland, Ohio 44106

CDC Surveillance

Lawrence B. Schonberger, M.D., M.P.H.
Centers for Disease Control and Prevention
Mail stop A-39
1600 Clifton Road, N.E.
Atlanta, GA 30333

National Cattlemen's Beef Association contacts:

Gary Weber, Ph.D.
National Cattlemen's Beef Association
1301 Pennsylvania Ave. N.W.
Suite 300
Washington, DC 20004
(202) 347-0228

Rick McCarty, APR
National Cattlemen's Beef Association
P.O. Box 3469
Greenwood Village, CO 80155
(303) 694-0305

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Glossary of Terms

Amyloid: naturally occurring proteins that appear as homogeneous aggregates or plaques under a light microscope, and as linear nonbranching aggregated fibrils arranged in sheets when seen under the electron microscope. Amyloids stain dark brown with iodine, produce a characteristic green color in polarized light after staining with Congo red, are metachromatic with either methyl violet (pink-red) or crystal violet (purple-red) and fluoresce yellow after thioflavine T staining.

Astrocytosis: an increase in the number, and often in the size, of astrocytes (one of the large neuroglia cells of nervous tissue) frequently observed in an irregular, poorly or moderately well-defined zone adjacent to degenerative lesions, focal inflammations or neoplasms in the brain.

Bovine Spongiform Encephalopathy (BSE): a degenerative disease affecting the central nervous system of cattle. BSE is found in the United Kingdom and other European countries.

Creutzfeldt-Jakob Disease (CJD): a rare neurological disease that usually afflicts persons over 55 years of age. CJD was first identified in the 1920s, and it occurs at a rate of about one person per million each year worldwide. It's important to note that this incidence rate represents an average over time. Because age is a key factor in evaluating CJD distribution, and because the disease tends to strike people over the age of 55, the actual rate is higher for ages 55 or older.

Electroencephalograph (EEG): a medical procedure that records and measures electrical activity in the brain and often is used to assist in the diagnosis of CJD.

Ruminant: cattle, sheep, goats, deer, elk and buffalo that, as a result of having four separate stomach chambers, are able to digest a wide

Immunohistochemistry: a laboratory methodology employed to detect the presence and distribution of an antigen (generally a protein). It is based on the use of specific antibodies coupled with a marker such as fluorescent dyes or enzymes. The technique has been used to detect the abnormal protein that accumulates throughout the course of BSE and other Transmissible Spongiform Encephalopathies or TSEs (see definition on the following page).

Immunoblot: a biochemical technique by which proteins are separated according to their molecular weight using electrophoresis and are detected with specific antibodies. Immunoblot is commonly used for the detection of abnormal PrP in brains of subjects suspected to have a TSE.

Plaque: a patch or small differentiated area of intense amyloid concentration seen on histopathologic examination of the brain.

PrP^c (prion protein cellular): a naturally occurring protein found in cells of central nervous system and other tissues. Changes in the structure of the protein result in an abnormal shaped protein (often referred to as PrP^{res} or PrP^{Sc}) that accumulates in the brains of subjects affected by a TSE disease. Some scientists believe that TSE diseases are caused solely by the abnormal protein, and they refer to these diseases as "prion" diseases. Other scientists believe that an infectious agent, such as a virus, causes the conversion of normal PrP to abnormal PrP.

Prion: name used by some but not all scientists to describe the causative entity of TSE diseases. A prion is a novel infectious particle that differs from bacteria, viruses, fungi, viroids and plasmids. It consists of one protein, is resistant to inactivation by most procedures that destroy biological agents such as heat, and shows heterogeneity with respect to size. Also referred to as protease resistant protein (PrP^{res}) or PrP Scrapie (PrP^{Sc}).

range of organic and plant foods, including grass and other forage.

Scrapie Associated Fibrils (SAF): term used to describe aggregated PrP^{res} or PrP^{Sc} as seen using electron microscopy.

Transmissible Spongiform Encephalopathy (TSE): name for a group of brain diseases that causes sponge-like abnormalities in brain cells. TSE diseases are associated with accumulation of abnormal PrP in the brain. All scientists agree that accumulation of the abnormal PrP results in altered function and eventual death of cells. Scientists do not know if a virus-like infectious agent causes normal PrP to convert to the abnormal form, or if abnormal PrP itself causes the conversion from normal protein to abnormal protein.

new variant CJD (nvCJD) or variant CJD (vCJD): name given to a newly identified human TSE which is significantly different from other forms of CJD. The number of definite and probable cases is 153 people (143 in the U.K., six in France, one in Ireland, one in Italy, one in the United States, and one in Canada. Scientists have concluded that the patients in the United States and Canada contracted nvCJD in the U.K.)*²² (Both nvCJD and vCJD refer to the same entity. nvCJD is used throughout this information resource primarily and is preferred by many experts; however, vCJD is also commonly used.)

* As of December 1, 2003.

Transmissible Spongiform Encephalopathies (TSE)

The Basic Facts

Transmissible Spongiform Encephalopathies (TSEs) are a class of rare brain diseases, some of which affect humans while others affect animals. TSEs are associated with the accumulation of abnormal prion protein (PrP) in the brain. This abnormal protease-resistant protein is referred to as PrP^{res} (protease resistant protein) or PrP^{Sc} (PrP Scrapie).

All mammals produce PrP in cells of the central nervous system and other tissues. Changes in normal PrP are believed to lead to an altered protein referred to by some scientists as a "prion" (proteinacious infectious particle). Scientists believe that when abnormal PrP comes in contact with normal PrP, it distorts the normal protein structure. Scientists do not know what factors trigger this conversion. Some believe the abnormal PrP itself causes the conversion, while others believe a virus-like entity may be involved. Most scientists agree that the accumulation of abnormal PrP in brain cells results in altered function and eventual death of cells. ^{1, 13-16}

Creutzfeldt-Jakob Disease (CJD) and New Variant Creutzfeldt-Jakob Disease (nvCJD) are distinctly separate TSEs, each with its own unique clinical and histopathological features.

CJD was first identified in the 1920s, and the Centers for Disease Control and Prevention (CDC) report the rate of CJD cases in the United States remains consistent with the rate in many other countries, which is approximately one case per million people each year. It's important to note that this incidence rate represents an average over time. Because age is a key factor in evaluating CJD distribution, and because the disease tends to strike people over the age of 55, the actual rate is higher for ages 55 or older. ^{2, 15}

New Variant CJD was first documented in the United Kingdom in 1996 and the number of definite and probable cases is 153 people (143 in the U.K., six in France, one in Ireland, one in Italy, one in the United States, and one in Canada. Scientists have concluded that the patients in the United States and Canada contracted nvCJD in the U.K.)^{*22} Surveillance by the CDC, in cooperation with state health departments and the National Prion Disease Pathology Surveillance Center, shows that no domestic cases of nvCJD have been detected in the U.S. ^{2, 15} A probable nvCJD case was reported in Spring 2002 in a British woman residing in Florida.

BSE, which is commonly referred to as "mad cow disease," has been detected in cattle in the U.K. and other European countries. A surveillance program conducted by the United States Department of Agriculture (USDA) since 1990 has found no cases of BSE in cattle in the United States. The USDA, Food and Drug Administration and many arms of the livestock industry have taken steps for nearly a decade to prevent BSE from ever occurring in the U.S. ³

The disease agent for BSE, to date, only has been found in brain tissue, the spinal cord and retina of naturally infected cattle. ^{** 1, 4, 9}

* As of December 1, 2003.

** Evaluation of experimentally inoculated cattle has found BSE infectivity in additional nervous and other tissues, specifically the dorsal root ganglia (nervous tissues connected to the spinal cord) and trigeminal ganglia (nervous tissue connected to the brain), as well as distal ileum (tissues in the intestines) and bone marrow. This research involved a series of experiments in which calves were either intracranially injected with or fed relatively large

amounts of heavily infected brain from clinical BSE cases. Examination of the animals fed BSE-infected brain showed infectivity in the distal ileum six to eight months after exposure and in other central nervous tissues 30 months or more after exposures. Reports on the research state that muscle meat and other tissues were tested for infectivity at every stage of these experiments, and no infectivity was found.²⁰

TSEs Affecting Animals	TSEs Affecting Humans
<p>Scrapie in sheep and goats Transmissible Mink Encephalopathy Chronic Wasting Disease in deer and elk* Bovine Spongiform Encephalopathy (BSE) TSEs in captive wild ruminants, cats, and monkeys in Europe are believed to have resulted from BSE-contaminated feed. Feline Spongiform Encephalopathy in Europe is also believed to have occurred in this way.</p>	<p>Creutzfeldt-Jakob Disease (CJD) Fatal Familial Insomnia Gerstmann-Sträussler-Scheinker Disease Kuru New variant CJD (nvCJD).</p>

* Chronic Wasting disease (CWD) is a contagious fatal TSE in cervids (members of the deer family). Research suggests that humans, cattle and other domestic livestock are resistant to natural transmissions. For more information on CWD, please visit these websites:

- *Chronic Wasting Disease Alliance*
- *USDA Animal and Plant Health Inspection Service
Colorado Division of Wildlife*

Creutzfeldt-Jakob Disease (CJD)

Discovery

Creutzfeldt-Jakob Disease was first identified in the 1920s by German neuroscientists Hans Gerhard Creutzfeldt and Alphonse Maria Jakob. Creutzfeldt had described a case of progressive fatal dementia in a female patient that was accompanied by multiple neurological abnormalities. Jakob described five similar cases. For many years, there was debate about the clinical and pathological features of such diseases, but by 1960, spongiform changes in brain tissue was accepted as the major pathological criteria for diagnosing CJD.¹³

Incidence

CJD affects approximately one person per million each year worldwide and usually strikes those over the age of 55 (median age of death is 68 in the U.S.¹¹). It's important to note that this incidence rate represents an average over time. Because age is a key factor in evaluating CJD distribution, and because the disease tends to strike people over the age of 55, the actual rate is higher for ages 55 or older.¹⁶

The global incidence of sporadic CJD cases has remained consistent throughout the world in those countries where it is being monitored. CJD affects men and women of diverse ethnic backgrounds and is always fatal.⁴

Transmission

CJD can occur in one of three forms:¹⁻⁴

- a familial, or genetically inherited form
- a sporadic form, which is of an unknown origin and accounts for roughly 85 percent of all CJD cases
- an iatrogenic, or acquired, form due to inadvertent exposure to CJD-contaminated equipment or material as a result of brain surgery, corneal grafts, dura mater grafts and through the use of human pituitary-derived growth hormones or gonadotrophin.

CJD and New Variant CJD are distinctly separate TSEs, each with its own unique clinical and histopathological features.

CJD in the United States

The occurrence of CJD in the United States remains consistent with the rate of CJD cases in

Symptoms

The typical early symptoms of sporadic CJD include poor concentration, lethargy, visual disturbance and unsteadiness when standing or walking. As the disease advances, agitation, dementia and muscle twitching (myoclonus) characteristically occurs. The median survival of CJD patients is just four months, and almost ninety percent (90%) of sporadic CJD patients die within the first year of the onset of symptoms. No cure is available for CJD.^{4, 5, 8}

Diagnosis

The preliminary diagnosis of CJD is made following a neurological evaluation and analysis of brain waves through an EEG (electroencephalograph) and examination of the cerebro spinal fluid to search for the presence of 14-3-3 protein.^{4, 6}

A more reliable and often definitive diagnosis in a living patient can be obtained through a brain biopsy and subsequent examination of brain tissue. In advanced cases, infected brains will appear spongy when viewed under a microscope due to a change in cells' structures. However, conducting brain biopsies on living patients solely to confirm a clinical diagnosis of CJD is difficult to justify given the risks, such as extradural hematoma or brain abscesses, the possibility of sampling unaffected tissue and the low chance that the procedure will result in any benefit to the patient.⁸

Definite diagnosis of CJD and other human TSEs is generally established by analysis of brain tissue obtained after death or autopsy. Neuropathological features of CJD include spongiform change, neuronal loss, astrocytosis and, more rarely, the absence of amyloid plaques in the cerebral cortex. Additional methodologies used to help confirm the diagnosis include immunohistochemistry, the immunoblot technique and other techniques that detect unique protein markers.^{4, 7, 12, 13}

many other countries, which is approximately one case per million people each year. It's important to note that this incidence rate

represents an average over time. Because age is a key factor in evaluating CJD distribution, and because the disease tends to strike people over the age of 55, the actual rate is higher for ages 55 or older. The Centers for Disease

Control and Prevention (CDC) monitors annual death rates for CJD cases in the U.S. has found that the national incidence rate has remained relatively stable since 1985 ¹¹.

Creutzfeldt-Jakob Disease Deaths and Incidence in the United States, 1979-1998			
Characteristics	Incidence ●	Risk Ratio (95% CI) ■	No. (%) of Deaths ♦
Age			
>55y	4.13	33.7 (30.7-37.1)	4274 (90.0)
<55y	0.12	Reference	477 (10.0)
Sex			
Male	1.06	1.2 (1.1-1.2)	2252 (47.4)
Female	0.90	Reference	2499 (52.6)
Race ♥			
White	1.03	Reference	4505 (95.8)
Other	0.67	0.7 (0.5-0.8)	74 (1.6)
Black	0.39	0.4 (0.3-0.5)	171 (3.6)
Region ♣			
Northeast	1.08	1.3 (1.2-1.4)	1195 (25.2)
Midwest	1.03	1.2 (1.1-1.3)	1270 (26.7)
West	0.93	1.1 (1.0-1.2)	869 (18.3)
South	0.85	Reference	1416 (29.8)
Period ♠			
1995-1998	1.03	Reference	1108 (23.3)
1991-1994	1.00	1.0 (0.9-1.0)	1027 (21.6)
1987-1990	0.98	0.9 (0.9-1.0)	964 (20.3)
1983-1986	0.95	0.9 (0.8-1.0)	886 (18.6)
1979-1982	0.86	0.8 (0.7-0.9)	766 (16.1)
US Total	0.97		4751 (100)

- Death rates are expressed per million persons.
 - Risk ratios with 95% confidence intervals (CIs) were calculated using Poisson regression analysis.
 - ♦ Race and region were unknown for 1 death.
- Age-adjusted death rates per million persons.
Age-race-adjusted death rates per million persons.

Source: Centers for Disease Control and Prevention, November 2000

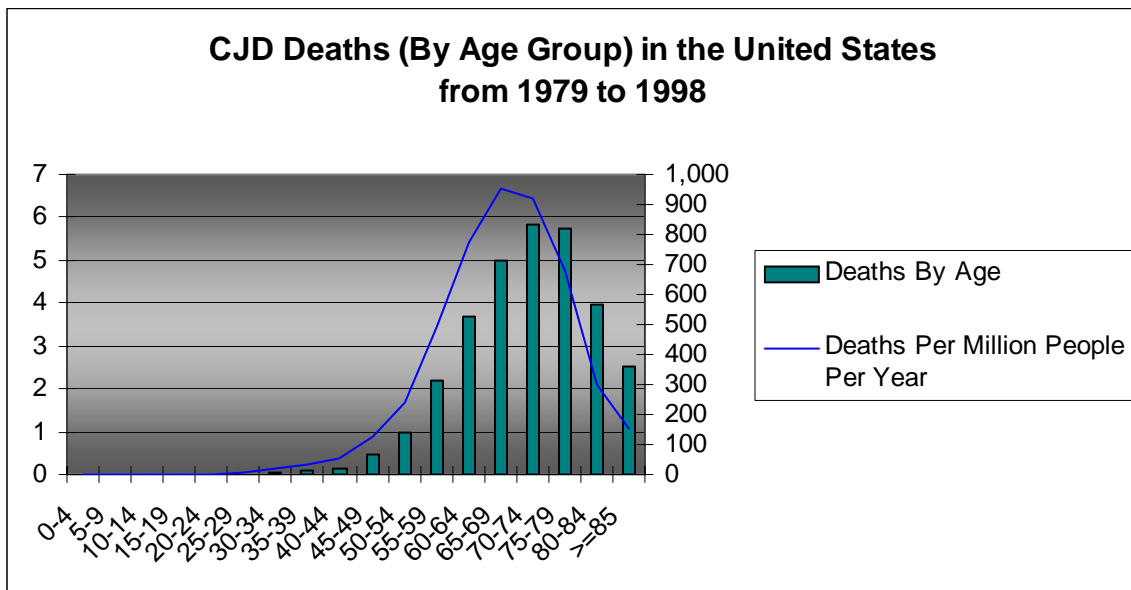
With heightened concern about nvCJD in the United Kingdom, the CDC enhanced its CJD surveillance using mortality data from 1979 through 1998. The CDC team has not seen an increase in the CJD death rate in recent data despite the extensive attention to the diseases. The average annual age-adjusted death rate was .97 deaths per million persons, ranging from .78 in 1980 to 1.13 in 1997, while the overall annual rate has been stable since 1985. The median age at death was 68 years, while the median age at death of patients with nvCJD

was 27.5 years.¹¹

An analysis by the University of California at San Francisco also found no sign of the New variant CJD in brain specimens from 67 CJD cases researchers there collected between 1991 and 1996.²

The CDC continues to conduct national surveillance to identify CJD cases in patients under the age of 55 through mortality data and in collaboration with state health departments.¹¹ It also reviews the available clinical and pathological records of these patients. In addition, the CDC worked with the American Association of Neuropathologists to alert its members about the neurological characteristics of nvCJD and request they report any suspected cases of nvCJD regardless of age or original clinical diagnosis.

To further improve surveillance and facilitate neuropathological study of suspected CJD cases, the American Association of Neuropathologists, with the support of the CDC, has established a National Prion Disease Pathology Surveillance Center.^{2, 15} The Internet address of the center is <http://www.cjdsurveillance.com>. Since 1997 the National Prion Pathology Surveillance Center has examined tissues from 597 cases of prion disease, without detecting a single case of nvCJD.



Source: Centers for Disease Control and Prevention, December 2000.

** CJD affects approximately one person per million each year worldwide and usually strikes those over the age of 55 (median age of death is 68 in the U.S.¹¹). It's important to note that this incidence rate represents an average over time. Because age is a key factor in evaluating CJD distribution, and because the disease tends to strike people over the age of 55, the actual rate is higher for ages 55 or older.¹⁶

Classifying Sporadic CJD Cases	
Definite =	cases in which the abnormal prion protein has been detected in brain tissue (Prion proteins June be detected using immunohistochemistry or immunoblot, or histology June illustrate spongiform changes. ^{3,4})
Probable =	patients with rapidly progressive dementia lasting less than two years, periodic sharp-wave complexes in EEG results and any two of the following neurological symptoms: myoclonus, visual and/or cerebral symptoms, pyramidal and/or extrapyramidal signs or akinetic mutism.
Possible =	those fulfilling the above criteria without typical EEG abnormalities.

Source: Global Surveillance, Diagnosis and Therapy of Human Transmissible Spongiform Encephalopathies: Report of a WHO Consultation. World Health Organization, Geneva, Switzerland, 9-11 February 1998.

Bovine Spongiform Encephalopathy (BSE)

Discovery

Reports of suspected clinical cases of BSE date back to 1985. However, the disease was not officially confirmed until November of 1986.^{1,3} More than 99 percent (99%) of BSE cases have been reported in cattle born in the United Kingdom. Ireland, France, Portugal, Belgium, the Netherlands, Luxembourg, Liechtenstein, Denmark, Switzerland, Germany, Spain, Italy, Greece, Czech Republic, Slovakia, Slovenia, Austria, Finland, Japan and Israel have reported cases of BSE in native cattle, but the incidence rate in these countries is significantly lower than in the U.K. It is believed by many scientists that cases in native cattle outside the U.K. likely resulted from the importation of feed which was contaminated with the BSE agent from Britain.¹⁵

Incidence

As of November 13, 2003, the total number of confirmed BSE cases in U.K. cattle was 183,191.²¹ The epidemic peaked in 1992-93 with almost 1,000 cases per week. Currently, approximately 30 cases per week are identified and this number continues to drop. BSE has not been identified in the United States. The United States Department of Agriculture (USDA) has monitored cattle in the U.S. for 13 years and has tested over 57,352 brain specimens (as of September 30, 2003) from cattle displaying any neurological symptoms that might indicate BSE. To date, the USDA has found no BSE cases among U.S. cattle.³ In addition, the USDA, the Food and Drug Administration (FDA) and many arms of the livestock industry have taken a number of measures over the years to prevent BSE from occurring in the U.S., including:

The United States has not imported beef from the U.K. since 1985.

In 1989, the U.S. banned the importation of ruminant animals and at-risk ruminant products from countries with confirmed cases of BSE.

Transmission

There are different scientific hypotheses concerning the origins of BSE. The epidemiological data suggest that BSE in the U.K. is an extended common source epidemic involving feed containing TSE-contaminated meat and bone meal (MBM) as a protein source. The causative agent is suspected to be from either Scrapie-affected sheep or cattle with a

Prior to these bans, 496 cattle were imported into the U.S. from the U.K. and Ireland between 1981 and 1989. These cattle have been tracked and closely monitored for years. Only one remains alive, and is being monitored by APHIS. Analysis of brain tissue from imported cattle that were tested showed no presence of any Transmissible Spongiform Encephalopathy, including BSE. In addition, of the 41 cattle imported from other European Countries in 1996-1997, only 5 remain alive and are under quarantine. No evidence of BSE has been found in any of these imported animals.

More than 60 veterinary diagnostic laboratories throughout the U.S. participate in a BSE surveillance program along with the National Veterinary Services Laboratory in Ames, Iowa.

On August 4, 1997, an FDA regulation went into effect banning the use of at-risk mammal-derived animal protein by-products in cattle feed to ensure that if the BSE disease agent ever entered the U.S. it would be prevented from spreading through cattle feed.

On December 12, 1997, the USDA banned imports of all live ruminants and at-risk ruminant products from Europe until risk factors associated with BSE are more fully examined.

On December 7, 2000, APHIS prohibited all imports of rendered animal protein products from Europe, regardless of species.

previously unidentified TSE.^{3,10} If this theory were true and BSE were to emerge in the United States, the FDA feed ban in the United States would be expected to reduce any amplification of the disease in cattle in this country.

Changes in rendering operations in the early 1980s, particularly the removal of a solvent

extraction process that included a steam heat treatment, may have played a part in the appearance of BSE and the subsequent amplification of the agent in the cattle population. Cases that have been detected in other countries appear to be a result of importation of live cattle or, more significantly, contaminated feed from the U.K.¹⁵ There is no evidence that BSE spreads horizontally (i.e., by contact between unrelated adult cattle and from cattle to other species). Limited evidence suggests that maternal transmission may occur at an extremely low level but that it would not perpetuate the epidemic under current British farming conditions. Research continues in this area.

Successful experimental infection of sheep with BSE has shown that sheep are also susceptible to BSE by the oral route. Thus, importation of sheep exposed to potentially BSE-contaminated protein concentrates in Europe are banned in the United States. In 2000, the United States Department of Agriculture initiated efforts to acquire about 375 sheep imported to Vermont from Europe in 1996, when no import ban on such sheep was in force. These flocks of sheep had been under quarantine since 1998 because of their potential exposure to BSE contaminated feed in Europe and, in 2000, four of these sheep were confirmed with an atypical Transmissible Spongiform Encephalopathy. The flocks were destroyed in March 2001, and tissue samples were collected for diagnostic testing. Results of strain typing of the agent infecting these sheep to determine whether the atypical agent is BSE is anticipated to take about two years. Currently, however, cattle remain the only known food animal species with disease caused by the BSE agent.

Clinical Signs

Cattle with BSE display gradual changes in several aspects of their behavior, including:

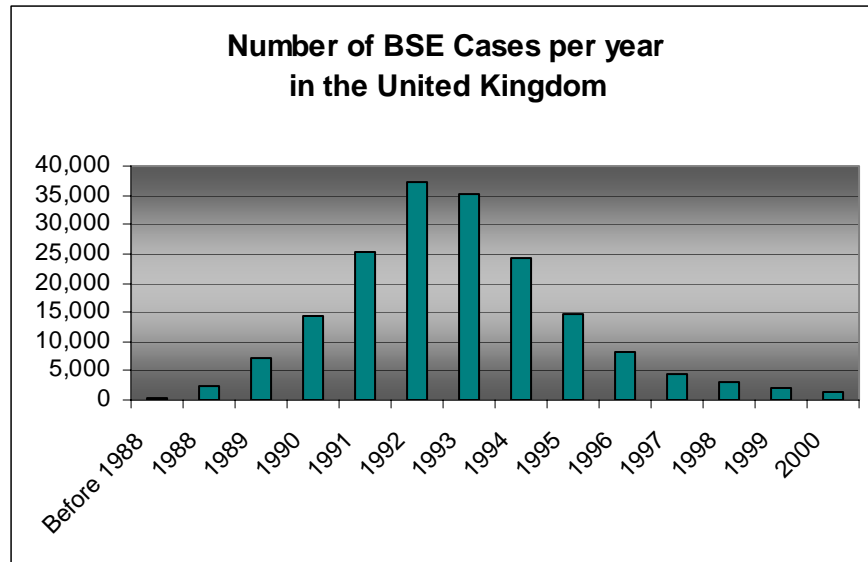
- temperament changes such as increased nervousness or aggression
- abnormal posture
- coordination problems
- difficulty in rising or walking
- decreased milk production
- severe muscular twitching
- loss of body weight despite a continued appetite

The incubation period for BSE ranges from two to eight years. Following the onset of clinical signs, the animal's condition rapidly deteriorates until it dies (usually within six months) or is destroyed. The disease is fatal, and there is no treatment or vaccine to prevent BSE.

Diagnosis/Diagnostic Tests

There currently are no proven practical tests available to detect the disease in live cattle. Several laboratories are in the process of developing new tests with practical applications, but these methods are still being evaluated. Farmers may suspect BSE based on a cow's behavior, but cases are confirmed only when veterinary pathologists perform microscopic examination of brain tissue.

There are also supplemental tests, which include detection of Scrapie Associated Fibrils (SAF) by electron microscopy or detection of PrP^{res} through immunohistochemistry, the immunoblot analysis and other techniques that detect unique protein markers.^{3,4}



Source: Office of International Epizootics/World Organization for Animal Health, April 2001. ²¹
http://www.oie.int/eng/info/en_esbru.htm

The long-awaited but controversial final BSE Inquiry Report in the U.K. released October 24, 2000 concluded that BSE probably originated from a novel source early in the 1970s, possibly a cow or other animal that developed the disease as a consequence of a gene mutation. The report asserts that the cases of BSE identified between 1986 and 1988 were not index cases, nor were they the result of the transmission of Scrapie. They were the consequences of recycling of cattle infected with BSE itself. The BSE agent was spread in meat-and-bone-meal (MBM). The origin of the disease will probably never be known with certainty. Other assertions from the report: the theory that BSE developed from changes in rendering methods has no validity, and that rendering methods have never been capable of completely inactivating TSEs; the theory that BSE is caused by application to cattle of organophosphate pesticides is not viable, although there is the possibility that these can increase the susceptibility of cattle to BSE; and the theory that BSE is caused by an autoimmune reaction is not viable. <http://www.bseinquiry.gov.uk/>

New Variant CJD (nvCJD)

Discovery

New variant Creutzfeldt-Jakob Disease (nvCJD) was first documented in March of 1996 after 10 Britons under the age of 45 displayed symptoms similar to those associated with a TSE. CJD was initially suspected as the specific disease, but further scientific analysis showed symptomatic and pathological differences of affected brain tissues compared with CJD victims. It was certain, however, that the 10 victims suffered from a strain of a Transmissible Spongiform Encephalopathy, and researchers termed this condition new variant CJD (nvCJD).

Incidence

The number of definite and probable new variant CJD cases is 153 people (143 in the U.K., six in France, one in Ireland, one in Italy, one in the United States, and one in Canada. Scientists have concluded that the patients in the United States and Canada contracted nvCJD in the U.K.).²² To date, the disease has occurred almost exclusively in people under the age of 55, a number of whom were teenagers.

Scientists do not believe it is possible to predict the number of anticipated nvCJD cases with any accuracy given the unknowns about the disease, including method and amount of exposure, route of transmission and incubation period. Steps taken to remove the disease agent should help minimize potential future exposure to the agent and thereby limit the occurrence of nvCJD cases.

Transmission

Recent research from the U.K. supports an association between BSE and vCJD, in that nvCJD likely developed as a result of people consuming products contaminated with central nervous system tissue of BSE-infected cattle. Documented studies report that the BSE agent, to date, only has been found in brain, spinal cord and retina (eye) tissue of naturally infected cattle. **

Additional research indicates that all nvCJD patients tested to-date have been homozygous for the amino acid methionine at codon 129, which is one of the amino acids on the gene that comprises PrP. Research continues to see if this commonality would indicate a genetic

predisposition to infection by the BSE agent.¹⁵⁻¹⁹

Symptoms

New Variant CJD differs markedly from CJD. Symptoms of nvCJD last up to 14 months, compared with 4 months for CJD patients. Patients afflicted with nvCJD experienced early psychiatric symptoms such as depression, earlier loss of coordination and later onset of dementia. In addition, nvCJD has, to date, occurred almost exclusively in people under the age of 55, a number of whom were teenagers, whereas CJD typically strikes people over 55.^{2, 8, 15, 18}

Diagnosis

Diagnostic procedures for nvCJD are similar to those of CJD, keeping in mind that patients with nvCJD lack periodic sharp-wave complexes typically found on EEG results of CJD patients. Perhaps the most striking and consistent neuropathological difference between CJD and nvCJD is found in the amyloid plaques. Plaques in nvCJD cases are extensively distributed throughout the cerebrum and cerebellum, compared with the absence of plaques in CJD cases. Plaques in nvCJD victims also typically have a dense center and are surrounded by a zone of spongiform change which give the plaques a daisy-like floral pattern. This pattern is not found in CJD patients.^{4, 6, 7, 9, 15, 20}

Recently, researchers developed a new test that may allow for an earlier diagnosis of nvCJD. Patients with nvCJD, but not CJD, appear to have detectable disease associated prion protein in their tonsils. By removing a small piece of tonsil tissue and analyzing it for the protein, researchers may now be able to provide a definite diagnosis of nvCJD at an earlier stage. No indigenous cases of nvCJD have been discovered in the U.S. A probable nvCJD case was reported in Spring 2002 in a British woman residing in Florida.

**As of December 1, 2003.*

*** Evaluation of experimentally inoculated cattle has found BSE infectivity in additional nervous and other tissues, specifically the dorsal root ganglia (nervous tissues connected to the spinal cord) and trigeminal ganglia (nervous tissue connected to the brain), as well as distal ileum (tissues in the intestines) and bone marrow. This research involved a series of experiments in which calves were either intracranially injected with or fed relatively large*

amounts of heavily infected brain from clinical BSE cases. Examination of the animals fed BSE-infected brain showed infectivity in the distal ileum six to eight months after exposure and in other central nervous tissues 30 months or more after exposures. Reports on the research state that

muscle meat and other tissues were tested for infectivity at every stage of these experiments, and no infectivity was found.²⁰

Differing Characteristics of Sporadic CJD and nvCJD	
CJD	nvCJD
<p>Discovery Identified by German psychiatrists Hans Gerhard Creutzfeldt and Alphonse Maria Jakob in the 1920s</p> <p>Incidence Affects approximately one person per million worldwide each year, representing an average over time that increases with age Usually strikes people over the age of 55 (median age of death is 68 in the U.S.¹¹)</p> <p>Transmission Sporadic form is of an unknown origin and accounts for about 85% of all CJD cases</p> <p>Symptoms Includes poor concentration, lethargy and unsteadiness followed by agitation, dementia and chronic muscle spasms Duration of the typical form of illness averages four months</p> <p>Diagnosis Sharp-wave complexes present in EEG in most cases Neuropathological features include spongiform change, neuronal loss, and astrocytosis.</p>	<p>Discovery First documented in March 1996 in Great Britain</p> <p>Incidence There are 153 definite and probable cases, (143 in the U.K., six in France, one in Ireland, one in Italy, one in the United States, and one in Canada. Scientists have concluded that the patients in the United States and Canada contracted nvCJD in the U.K.) as of December 1, 2003²²</p> <p>Disease has stricken almost exclusively people under the age of 55, a number of whom were teenagers There have been no indigenous cases reported in the United States. A probable nvCJD case was reported in Spring 2002 in a British woman residing in Florida.</p> <p>Transmission Research from the U.K. supports an association between BSE and nvCJD in that nvCJD likely developed as a result of people consuming products contaminated with nervous system tissue from BSE-infected cattle</p> <p>Symptoms Patients experience early psychiatric symptoms, earlier loss of coordination and later onset of dementia Duration of illness averages about 14 months</p> <p>Diagnosis Lack sharp-wave complexes in EEG results Amyloid plaques are extensively distributed throughout the cerebrum and cerebellum Plaques typically have a dense center surrounded by spongiform change that give the plaque a daisy-like floral pattern</p>

Timeline

<i>Timeline of Prevention Measures and Other Developments in the Fight Against BSE</i>	
1985	Due to risks other than BSE, no U.K. processing plants were approved to export British beef into the United States. Consequently, the U.S. has not imported beef from the UK since 1985.
November 1986	BSE is first diagnosed in the U.K.
July 18, 1988	Ruminant meat and bone meal (MBM) is banned from inclusion into cattle feed in the U.K.
July 21, 1989	USDA/APHIS bans the importation of ruminant animals (cattle, sheep, goats, deer, elk and buffalo) from countries with confirmed cases of BSE.
November 1989	USDA/APHIS enacts emergency ban on the importation of at-risk ruminant products (including meat-and-bone-meal) from countries with confirmed cases of BSE. Formal regulation to follow.
1990	FDA intensifies microbiological review of new drug applications for human drug products derived from bovine sources. USDA initiates a surveillance program and begins testing for BSE in cattle from high-risk populations (older animals and those showing signs of possible neurological disease).
December 6, 1991	USDA/APHIS enacts formal regulation to restrict the importation of ruminant meat and edible products, and bans at-risk by-products of ruminant origin from countries known to have BSE.
1993	USDA/APHIS expands BSE surveillance program to include examination of brain tissue from non-ambulatory or "downer" cows.
January 1993	BSE epidemic in U.K. peaks with 1,000 new cases reported per week.
1994	USDA/APHIS implements immunohistochemistry testing method for BSE.
March 20, 1996	British government announces possible link between BSE and 10 cases of a new human TSE called new variant Creutzfeldt-Jakob Disease (nvCJD).
March 29, 1996	National livestock organizations and professional animal health organizations in the U.S. announce a voluntary program to discontinue the use of ruminant-derived protein in ruminant feed. The FDA and USDA announce their intentions to determine if additional regulations are necessary to prevent the introduction and or amplification of the BSE agent in the United States.

January 1997	FDA proposes a ban on the use of ruminant products in livestock feed.
June 2, 1997	FDA issues a regulation banning the use of at-risk mammalian protein in animal feed. Limited exceptions include blood, milk or gelatin products, and equine and porcine protein, which is derived from species not known to develop TSEs naturally.
August 4, 1997	FDA rule that banned the use of at-risk mammal-derived protein by-products in bulk feeds for cattle becomes effective.
October 3, 1997	FDA rule that banned the use of at-risk mammal-derived protein by-products in bagged feed for cattle becomes effective.
December 12, 1997	USDA/APHIS bans imports of all live ruminants and at-risk ruminant products from Europe until risk factors associated with BSE are more fully examined.
April 24, 1998	USDA/APHIS enters into a cooperative agreement with Harvard University's School of Public Health to analyze and evaluate the USDA's BSE prevention measures.
March 2000	Due to concerns about foot-and-mouth disease, U.S. restricts imports of live ruminants and animals from Japan. Restrictions continue as the first case of BSE found outside of Europe is diagnosed in Japan, in September 2001. The ban from March 2000 was never lifted.
July 14, 2000	The U.S. Secretary of Agriculture issues a Declaration of Extraordinary Emergency after four sheep in Vermont test positive for a Transmissible Spongiform Encephalopathy (TSE). The sheep came from one of three flocks that have been quarantined by the state of Vermont since 1998 after learning the sheep may have been exposed to BSE-contaminated feed in Belgium and the Netherlands, from where they originated. One of three flocks (21 sheep) were voluntarily relinquished and destroyed. Diagnostic samples were taken for testing and the possibility of further research. The other two flocks remained under quarantine until March 2001 at which time they were destroyed.
December 7, 2000	APHIS prohibits all imports of rendered animal protein products from Europe, regardless of species.
January 29, 2001	The National Cattlemen's Beef Association hosts meeting with the FDA Center for Veterinary Medicine, USDA Animal and Plant Health Inspection Service, the feed industry and meat packing and rendering industries to discuss ensuring full compliance with FDA rulings.
February 3, 2001	Officials from the NCBA, Canadian Cattlemen's Association and Conferacion Nacional Ganadera of Mexico sign a joint statement pledging to keep BSE out of North America.

March 21 & 23, 2001	USDA, under the authority of the U.S. District Court, removes two remaining quarantined flocks (234 sheep and 126 sheep) from private farms in Vermont. Tissue samples are collected for diagnostic testing and the sheep are destroyed.
April 2001	U.S. beef industry implements an affidavit system by which cattle producers provide written confirmation that cattle posted for sale have not been fed prohibited materials per the 1997 feed ban regulations. The U.S. feed industry develops a certification program, which assures that certified feed suppliers comply with FDA feed ban regulations.
Fall 2001	USDA announces enhancements to its cattle surveillance system, including dividing the country into eight regions to assure testing accounts for regional differences yet assures uniform national surveillance. With this regional structure, USDA will double the number of cattle tested for BSE in 2002 as compared to the previous year.
November 2001	Harvard Center for Risk Analysis releases its BSE risk assessment study commissioned by the federal government. The report finds the risk of BSE ever occurring in the U.S. is "very low."
January 2002	President Bush announces his FY2003 Budget Proposal, which includes \$146 million in new spending to further protect the nation's food supply, strengthen food safety programs and support additional research.
February 2002	The beef industry develops an affidavit form for feed suppliers to certify that the feeds sold to cattle producers contain no prohibited materials.
April 2002	USDA announces that 2 of the samples for the destroyed Vermont sheep have tested positive for "an atypical undifferentiated TSE of foreign origin." Ongoing testing continues to determine the type of TSE.

Documented BSE Cases Worldwide*



Documented Cases in Europe

United Kingdom, 183,191**	Denmark, 13
Ireland, 1325	Slovakia, 12
France, 849	Poland, 9
Portugal, 835	Czech Republic, 8
Switzerland, 450	Slovenia, 3
Spain, 361	Liechtenstein, 2
Germany, 295	Luxembourg, 2
Belgium, 121	Greece, 1
Italy, 88	Finland, 1
Netherlands, 70	Austria, 1

Documented Cases Outside of Europe

Japan, 9	Australia, 0
Israel, 1	New Zealand, 0
Canada, 1	South America, 0
Africa, 0	United States, 0

Cases of BSE also have been confirmed in cattle imported from the U.K. to the following countries:

- Canada (1)
- Falkland Islands (1)
- Oman (2)

**The United Kingdom is comprised of Great Britain, Northern Ireland, Isle of Man, Jersey and Guernsey. Figure through November 13, 2003.

Source: Office of International Epizootics, December 15, 2003. ²¹ http://www.oie.int/eng/info/en_esb.htm

Recent Research

CJD and nvCJD U.S. Tracking

With heightened concern about nvCJD in the United Kingdom, the U.S. Centers for Disease Control and Prevention (CDC) enhanced its CJD surveillance using mortality data from 1979 through 1998. The CDC team has not seen an increase in the CJD death rate in recent data despite the extensive attention to the diseases. The average annual age-adjusted death rate was .97 deaths per million persons, ranging from .78 in 1980 to 1.13 in 1997, while the overall annual rate has been stable since 1985. The median age at death was 68 years, while the median age at death of patients with nvCJD was 27.5 years. Given the age difference between persons afflicted with CJD and nvCJD, the CDC enhanced its follow-up investigation of CJD patients younger than 55 years and established the National Prion Disease Pathology Surveillance Center (NPDPSC) in collaboration with the American Association of Neuropathologists. As of September 20, 2000, none of the CJD surveillance efforts detected any evidence of nvCJD in the United States.

Source: Research letter in JAMA November 8, 2000; 284:18. Gibbons RV, Holman RC, Belay ED, Schonberger LB, Division of Viral and Rickettsial Diseases, National Center for Infectious Disease, Centers for Disease Control and Prevention, Atlanta, Ga.

TSE Agent

Findings of a study by Dr. Stanley Prusiner and colleagues provides the most compelling evidence to date that prions from cattle with BSE have infected humans and caused new variant Creutzfeldt-Jakob (nvCJD) disease in humans. The team of scientist reports that transgenic mice expressing bovine prion protein serially propagate BSE prions and that there is no species barrier for transmission from cattle to these transgenic mice. Transgenic mice were injected with nvCJD and BSE brain extracts and with natural sheep Scrapie. The incubation times, neuropathology and prion proteins in mice inoculated with nvCJD and BSE were indistinguishable, but differed dramatically from those seen in the mice infected with natural Scrapie prions.

Source: Scott MR, Will RG, Ironside JW, Nguyen HB, Tremblay P, DeArmond SJ, Prusiner SB. Compelling transgenic evidence for transmission of bovine spongiform encephalopathy prions to humans. Proceedings of the National Academy of Sciences December 21, 1999; 26: 15137-15142.

Research conducted on Scrapie-infected mice by Charles Weissmann of the Imperial College School of Medicine in London suggests that prions appear to be produced by immune cells in the spleen known as follicular dendritic cells (FDCs). Formation and maintenance of FDCs requires the presence of B cells expressing membrane-bound lymphotoxin- α . The research team was able to stop the development of mature FDCs by using a soluble lymphotoxin- α receptor, which seemed to soak up the lymphotoxin from the B cells and stopped them from nurturing the FDCs that produce prions. The study showed that this treatment abolishes splenic prion accumulation and retards neuroinvasion after intraperitoneal Scrapie inoculation. These data provide evidence that FDCs are the principal sites for prion replication in the spleen. The researchers believe the prions enter the nerves in the spleen, then travel to the spine and to the brain.

Source: Montrasio F, Frigg R, Glatzel M, Klein MA, Mackay F, Aguzzi A, Weissmann C. Impaired prion replication in spleens of mice lacking functional follicular dendritic cells. Science June 19, 2000; 288: 1257-1259.

Transmission/Treatment

Richard Race and a team of researchers at the Laboratory of Persistent Viral Diseases, Rocky Mountain Laboratories, National Institutes of Health, Hamilton, Mont., and the Division of Virology, Department of Neuropharmacology, Scripps Research Institute, La Jolla, Cal., suspect naturally occurring TSEs such as BSE are probably transmitted by oral or other peripheral routes of infection. After infecting transgenic mice with hamster Scrapie orally or intraperitoneally, hamster prion protein (PrP) in peripheral nerves was sufficient for successful infection of the brain, and spleen cells were not required either to amplify or transport infectivity. Foreign PrP's role in interfering with Scrapie infection also was studied. Peripheral expression of heterologous PrP completely protected the majority of orally/intraperitoneally infected mice from clinical disease. Such

extensive protection has not been seen in earlier studies on interference, and these results suggest gene therapy with mutant PrP may be effective in preventing TSE diseases.

Source: Race R, Oldstone M, Chesebro B. Entry versus blockade of brain infection following oral or intraperitoneal scrapie administration: Role of prion protein expression in peripheral nerves and spleen. Journal of Virology January 2000; 828-833.

A study led by Jonathan Weissman and his colleagues from the University of California at San Francisco found that prions, and not some other unknown molecule, cause brain-destroying diseases such as CJD. Previous thinking held that other molecules besides prions (including sugars, other proteins and lipids) contributed to these infections. However, Weissman and his team isolated pure, infectious prions and introduced them into yeast cells which caused the yeast's own proteins to clump together. When the yeast divided, each new cell contained the misshapen prion-like proteins, but could not infect other species of yeast.

Source: Sparrer HR, Santoso A, Szoka Jr FC, Weissman JS. Evidence for the prion hypothesis: Induction of the Yeast [PSI⁺] factor by in vitro-converted Sup35 protein. Science July 28, 2000; 289: 595-599.

A new study reports transmission of BSE by blood transfusion in sheep and suggests the possibility that blood from human beings in the symptom-free stages of nvCJD could transmit infection to blood transfusion recipients. Nineteen transfusions from BSE-challenged UK Cheviot sheep to Cheviot sheep from a Scrapie-free flock of New Zealand-derived sheep created BSE clinical signs and pathological changes in one recipient of blood from a BSE-infected animal. While the study is still underway and will be for several years, the study indicates that BSE can be transmitted between individuals of the same species by whole-blood transfusion.

Source: Houston F, Foster JD, Chong Angela, Hunter N, Bostock CJ. Transmission of BSE by blood transfusion in sheep. The Lancet September 16, 2000: 356.

Pathogenesis

New research from the U.K. suggests that current definitions of the species barrier need to be fundamentally reassessed. Laboratory research with hamsters and mice demonstrate the existence of subclinical forms of prion infection. The researchers found that a strain of hamster prions thought to be nonpathogenic for

conventional mice leads to prion replication at high levels in such mice but without causing clinical disease. Prions pathogenic in both mice and hamsters are produced. This suggests the existence of subclinical forms of prion infection. This could have public health implications, both with respect to iatrogenic transmission from apparently healthy humans and dietary exposure to cattle and other species exposed to bovine encephalopathy prions.

Source: Hill AF, Joiner S, Linehan J, Desbruslais M, Lantos PS, Collinge J. Species-barrier-independent prion replication in apparently resistant species. Proceedings of the National Academy of Sciences 2000; 18: 10248-10253.

Modeling the Epidemic

The Scientific Steering Committee developed the Geographical BSE-Risk (GBR) as a qualitative indicator of the likelihood of the presence of one or more cattle being infected with BSE, pre-clinically or clinically, at a given point in time in a country. Where presence is confirmed, the GBR gives an indication of the level of infection. The report is limited to bovines and feed-based transmission of BSE and to countries that provided data for the assessment (14 EU Member States and nine third countries). The SSC labeled each country according to level of likelihood: Level I – highly unlikely; Level II – unlikely but not excluded; Level III – likely but not confirmed or confirmed at lower level; Level IV – confirmed at higher level. Correspondingly, the UK and Portugal are the only Level IVs, Austria/Finland/Sweden are the EU's Level IIs and the remaining participating EU countries received Level III ratings. The majority of "third countries" were assessed as Is, except for Switzerland which was considered a III and Canada and the US which were considered IIs because of small, non-negligible external challenges combined with more or less stable systems. More than anything, the report shows the dramatic shift in awareness and effective containment measures from the 1980s to the early 1990s. The report suggests using this assessment to modulate the use of meat or other bovine derived products based on their food/feed and non-food/feed uses.

Source: Final Opinion of the Scientific Steering Committee on the Geographical Risk of Bovine Spongiform Encephalopathy (GBR). Adopted July 6, 2000. http://europa.eu.int/comm/food/fs/sc/ssc/out113_en.pdf.

Summary of Facts

CJD – BSE – nvCJD

There is a family of diseases known as Transmissible Spongiform Encephalopathies (TSEs). Some TSEs affect animals and others affect humans. While Creutzfeldt-Jakob Disease (CJD), Bovine Spongiform Encephalopathy (BSE) and new variant CJD (nvCJD) belong to the TSE family, they are separate diseases, each with its own unique features. Details about CJD, BSE and nvCJD follow:

About CJD

CJD is a rare neurological disease that usually affects people over the age of 55 (median age of death is 68 in the U.S.)¹¹. It is important to note that studies at the Institute of Animal Health in Edinburgh and at the Imperial College of Medicine in London found that the BSE infectious agent has distinct features from the infectious agent of the classic CJD but similar to those of the nvCJD agent. CJD was first identified in the 1920s, while BSE was not identified until 1985.

CJD affects approximately one person per million each year worldwide. It's important to note that this incidence rate represents an average over time. Because age is a key factor in evaluating CJD distribution, and because the disease tends to strike people over the age of 55, the actual rate is higher for ages 55 or older. Surveillance of CJD cases by the Centers for Disease Control and Prevention (CDC) has found that the national incidence rate of CJD in the United States has remained relatively stable since 1985.

CJD affects men and women of diverse ethnic backgrounds, and it has been diagnosed in vegetarians and meat-eaters alike. It also has been reported in countries where BSE has never occurred.

There is no scientific evidence indicating CJD is caused by BSE. CJD results when abnormal protein accumulates in brain cells. Scientists do not know what factors trigger the conversion from normal protein to the abnormal form. Some believe the conversion is caused by a spontaneous mutation of the normal protein itself, while other scientists believe a virus-like entity may be involved.

About BSE

First identified in 1985, BSE is a degenerative disease affecting the central nervous system of cattle. Commonly known as "mad cow disease," BSE has not been found in the U.S., but it has been detected in the United Kingdom and several other countries.

Research from the U.K. indicates that the BSE disease agent has been found in brain tissue, the spinal cord and retina (eye) tissue of naturally infected cattle. It has not been detected in muscle meat or milk.

A surveillance program begun in 1990 by the United States Department of Agriculture (USDA) has found no evidence of BSE in U.S. cattle. In addition, the USDA, the Food and Drug Administration and many arms of the U.S. livestock industry have taken a number of measures for nearly a decade to prevent BSE from occurring in the U.S.

About nvCJD

Recent research from the U.K. does support an association between nvCJD and BSE. The human disease nvCJD likely developed as a result of people consuming products contaminated with central nervous system tissue from cattle infected with BSE.

CDC's monitoring efforts, in collaboration with state health departments, has not found evidence of indigenous cases of nvCJD in the U.S. A probable case of nvCJD was reported in Spring 2002 in a British woman residing in Florida.

CJD and nvCJD are distinctly separate diseases, each with its own unique features.

Questions and Answers

Q1. Is it possible for humans to get CJD from eating beef products?

A1. No, there is no scientific evidence linking classic CJD to diet. While the exact cause of classic CJD is unknown, scientists suspect that, like all Transmissible Spongiform Encephalopathies, classic CJD occurs when normal protein structures in the brain known as PrP change to an abnormal form. As abnormal PrP accumulates, it destroys neurons and results in brain damage. Classic CJD was first identified in the 1920s while BSE was not identified until 1985. Classic CJD occurs at a consistent rate of one person per million each year worldwide. It's important to note that this incidence rate represents an average over time. Because age is a key factor in evaluating classic CJD distribution, and because the disease tends to strike people over the age of 55, the actual rate is higher for ages 55 or older.

Q2. Is nvCJD caused by eating products from cattle infected with BSE?

A2. Recent research supports an association between BSE and nvCJD. The most likely source of human exposure was consumption of products containing brain or spinal cord tissue from BSE-affected cattle. To date, the BSE disease agent has not been found in muscle meat or milk, which comprise the majority of cattle products.

Q3. How many more cases of nvCJD are expected?

A3. No one can accurately predict how many more cases of nvCJD will occur because of the unknowns of the disease, including the amount and method of exposure, route of transmission and incubation period. Steps taken to remove the BSE disease agent should help minimize potential exposure and thereby limit the occurrence of nvCJD.

Q4. Does CJD occur in the U.S.?

A4. Yes. Classic CJD occurs in the U.S, but no indigenous cases of nvCJD have been identified. The occurrence of classic CJD in the U.S. remains consistent with the global rate of approximately one case per million people each year. It's important to note that this incidence rate represents an average over time. Because age is a key factor in evaluating classic CJD distribution, and because the disease tends to strike people over the age of 55, the actual rate is higher for ages 55 or older. Ongoing surveillance of classic CJD cases in the U.S. has been performed by the Centers for Disease Control and Prevention (CDC) since 1979. The CDC has found that the national incidence rate of CJD cases has remained relatively stable. The CDC also has found no evidence of indigenous cases of nvCJD in the U.S. Since 1997 the National Prion Pathology Surveillance Center has examined tissues from 597 cases of prion disease, without detecting a single indigenous case of nvCJD. A probable nvCJD case was reported in Spring 2002 in a British woman residing in Florida.

Q5. Has BSE ever been found in the U.S.?

A5. No. The USDA has conducted a BSE surveillance program in the U.S. for 13 years and has tested over 57,362 brain specimens from cattle displaying any neurological symptoms and from non-ambulatory animals (downer cows) that might indicate BSE. No cases have been found to date.

Q6. Is it possible BSE may be detected in the U.S. in the future?

A6. While no one can predict the future, the possibility of finding BSE in the United States is becoming more and more remote. The USDA, the Food and Drug Administration (FDA) and many arms of the national livestock industry have taken numerous steps to prevent BSE from ever occurring in the U.S., including: The United States has not imported any beef from the U.K. since before 1985.

In 1989, the U.S. banned the importation of ruminant animals and at-risk ruminant products from countries with confirmed cases of BSE in native cattle.

Prior to these bans, 496 cattle were imported into the U.S. from the U.K. between 1981 and 1989. These cattle have been tracked and closely monitored for years. Only one remains alive, and is quarantined. Analysis of brain tissue from imported cattle that were tested showed no presence of any TSE, including BSE. In addition, of the 41 cattle imported from other countries in 1996-1997, only 5 remain alive and are under quarantine.

More than 60 veterinary diagnostic laboratories throughout the U.S. participate in a BSE surveillance program along with the National Veterinary Services Laboratory in Ames, Iowa.

On August 4, 1997, an FDA regulation went into effect banning the use of at-risk mammal-derived animal protein by-products in cattle feed to ensure that if the BSE disease agent ever entered the U.S. it would be prevented from spreading through cattle feed.

On December 12, 1997, the USDA banned imports of all live ruminants and certain ruminant products from European countries until BSE is more fully understood.

On April 24, 1998, the USDA entered into a cooperative agreement with Harvard University's School of Public Health to analyze and evaluate the USDA's BSE prevention measures.

On December 7, 2000, APHIS prohibited all imports of rendered animal protein products from Europe, regardless of species.

Q7. Has nvCJD ever been found in the U.S.?

A7. Ongoing surveillance by the Centers for Disease Control and Prevention, in collaboration with state health departments, has found no indigenous cases of nvCJD in the U.S. A probable nvCJD case was reported in Spring 2002 in a British woman living in Florida.

Q8. Is it possible an indigenous case of nvCJD may be found in the U.S. in the future ?

A8. It is possible that a U.S. citizen might contract nvCJD if that person has traveled to or previously lived in countries where cases of BSE have been confirmed, and if that person consumed products containing brain or spinal cord from cattle infected with the BSE disease agent. There has never been a case of nvCJD that did not have a history of exposure within a country where BSE was occurring. The United States does not have BSE.

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Suggested Studies

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Information Resources

National Prion Disease Pathology Surveillance Center
Institute of Pathology
Division of Neuropathology
Case Western Reserve University
2085 Adelbert Road
Cleveland, OH 44106
(216) 368-0587
<http://www.cjdsurveillance.com/>

For additional information about this document, contact:

National Cattlemen's Beef Association
P.O. Box 3469
Englewood, CO
80155
(303) 694-0305
bseinfo@beef.org

Materials also are available on the Internet at <http://www.bseinfo.org>.