

Bovine Spongiform Encephalopathy

Mad Cow Disease, BSE

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Importance

Bovine spongiform encephalopathy (BSE) is a fatal neurodegenerative disease, caused by a prion, that mainly affects cattle. Other ruminant species, cats and humans are occasionally affected; this disease is called feline spongiform encephalopathy (FSE) in cats, and variant Creutzfeldt–Jakob disease (vCJD) in humans. BSE is a relatively new disease that was first reported in the United Kingdom in the 1980s. It is spread by ingestion; animals or humans become infected when they eat prion-containing tissues from an infected animal. Cooking and standard disinfection procedures do not destroy this agent. Infected animals or people do not become ill for years; however, the disease is always progressive and fatal once the symptoms develop.

The origins of BSE are unknown; however, the recycling of ruminant proteins in ruminant feed amplified this prion and caused an explosive epidemic in the U.K in the 1980s and 1990s. This epidemic peaked in 1992, with almost 1,000 new cases diagnosed each week, but has subsided as the result of control measures. BSE also spread to many European countries, North America, parts of Asia and possibly other areas of the world. The prevalence of disease varies widely between nations. As of August 2007, three cases had been reported in the U.S.: one case occurred in an imported animal and two in indigenous cattle. The presence of BSE in a country can result in trade sanctions, as well as increased public concern about meat safety. Many nations, including the U.S., are conducting control and surveillance programs. Most countries have also passed new regulations to prevent BSE-containing tissues from entering human or animal food supplies.

Etiology

BSE is a member of the transmissible spongiform encephalopathies (TSEs), a group of neurodegenerative disorders caused by unconventional disease agents. These agents are resistant to the treatments that ordinarily destroy bacteria, spores, viruses and fungi. They are generally thought to be prions, although a minority opinion suggests that TSEs may be caused by viruses or retroviruses. Prions are infectious proteins that appear to replicate by converting a normal cellular protein into copies of the prion. The cellular protein, which is called PrP^c, is found on the surface of neurons. Pathogenic isoforms of PrP^c are designated PrP^{res}; PrP^{Sc} or PrP^{TSE} are other names for this protein. Prions that cause different diseases (e.g. BSE or scrapie) are considered to be different strains of PrP^{res}.

In addition to the 'classical' BSE prion, at least two atypical BSE prions can be found in cattle. One has higher molecular mass fragments than classical BSE and is called 'H-type'; the other has a lower molecular mass and is called 'L-type' or bovine amyloidotic spongiform encephalopathy (BASE). Atypical BSE prions may represent additional strains of BSE or spontaneously occurring prions.

Geographic Distribution

Cases of BSE have been reported in indigenous cattle in most European countries, Canada, the U.S., Israel and Japan. This disease was seen in imported cattle in the Falkland Islands and Oman. Some countries including Iceland, Australia and New Zealand appear to be free of BSE; however, the presence or absence of this disease cannot be determined in countries without adequate surveillance programs.

Atypical BSE prions have recently been reported in Europe, the U.S. and Japan.

Transmission

BSE is usually transmitted when an animal or human ingests tissues containing the BSE prion. The prions are thought to replicate initially in the Peyer's patches of the ileum, then are transported via the peripheral nerves to the central nervous system (CNS). In cattle, prions can accumulate in the brain as early as 24 months after infection. The risks of transmission from various tissues are still incompletely understood; however, the highest prion concentration occurs in the CNS and ileum. In naturally infected cattle, BSE prions have been found mainly in the brain, spinal cord, retina and distal ileum, but more sensitive techniques have recently detected this agent

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in the dorsal root ganglia, peripheral nerves and adrenal glands. In experimentally infected cattle, it has been reported from the CNS, dorsal root ganglia, trigeminal ganglion, thoracic ganglia, some peripheral nerves, distal ileum (particularly in the Peyer's patches), adrenal glands, tonsils and bone marrow. Unpublished data suggest that BSE prions may also occur in the lymphoid tissues of nictitating membranes. Some tissues may contain prions only in the late stages of the disease; the accumulation of prions in the peripheral nerves and adrenal gland seems to coincide with or follow prion accumulation in the CNS. BSE has not been found in muscle; however, meat could become contaminated with CNS tissues during slaughter or processing. For this reason, high-risk slaughter and processing techniques have been banned in many nations (see Control). Epidemiological evidence and transmission studies suggest that BSE is not transmitted in milk, semen, or embryos.

There is little or no evidence that BSE is transmitted horizontally between cattle, but the offspring of infected animals have an increased risk of developing this disease. The route of transmission is unknown. If it occurs, vertical transmission seems to be rare. For this reason, some authors suggest that prions probably spread from cows to their calves soon after birth. Young animals may be particularly susceptible to infection; some studies suggest that most cattle become infected with BSE during the first six months of life.

BSE transmission in experimentally infected sheep resembles transmission in cattle, but the prions are more widely disseminated in the body, and additional routes of transmission may occur. In sheep inoculated orally, BSE prions are readily found in many lymphoid tissues including the spleen, lymph nodes and gut-associated lymphoid tissue (GALT), as well as in the CNS. Blood-borne transmission has been demonstrated in this species. Transmission from two ewes to their lambs occurred in an experimental flock; it is not known whether this event took place *in utero* or soon after birth.

In humans, variant Creutzfeldt-Jakob disease usually results from the ingestion of BSE prions, but iatrogenic routes of transmission are also possible. Probable human-to-human spread has been reported in several patients who received blood transfusions from asymptotically infected individuals. Other iatrogenic routes of transmission may be possible, including transmission in transplants or by contaminated equipment during surgeries. Prions can be found in the brain, spinal cord, dorsal root ganglia, trigeminal ganglia, retina, optic nerves and lymphoid tissues of humans with vCJD. Although prions are particularly common in the spleen and the tonsils, appendix and other gut-associated lymphoid tissues (GALT), they can also be found in lymph nodes throughout the body. Prions have been found in the appendix as early as two years before the onset of clinical disease. They have not been

demonstrated in human blood, but this may be due to the insensitivity of the assays used to detect these agents. Person to person transmission of vCJD does not occur during casual contact.

Origins of the BSE epidemic

The origins of BSE are not well understood. This disease was first reported in the 1980s, but it was probably present in cattle since the 1970s or earlier. The two most popular hypotheses are that BSE originated as a spontaneous PrP^c mutation in cattle, or that it came from a mutated scrapie prion that contaminated ruminant feed. Other sources suggest that BSE might have originated from a wildlife population or a human TSE agent. Once this agent entered cattle populations, it was amplified by recycling tissues from infected cattle into ruminant feed supplements, mainly as meat-and-bone meal (MBM). MBM is a rendered concentrate derived from animal offal and carcasses. Rendering cannot completely inactivate prions, but the epidemic may have been facilitated by changes in rendering practices that allowed more prions to survive.

Banning ruminant tissues from ruminant feed has significantly reduced the number of new cases of BSE, but cases have been reported in cattle born after these regulations came into effect ("born-after-the-ban" cases). These cases might be caused by illegal feeding of ruminant proteins or cross-contamination of cattle feed with swine or poultry feed. Theoretical possibilities include inadequate heating of bone meal or tallow used in concentrates and milk replacers, horizontal transmission or environmental reservoirs. Current diagnostic techniques are not sensitive enough to detect very low levels of prions, and there is little information on prion survival in the environment. However, hamster-adapted scrapie prions have been shown to survive in the soil for at least three years.

Disinfection

Decontamination of prion-contaminated tissues, surfaces and environments is difficult. These agents are highly resistant to most disinfectants (including formalin), heat, ultraviolet radiation and ionizing radiation, particularly when they are protected in organic material or preserved with aldehyde fixatives, or when the prion titer is high. Prions can bind tightly to some surfaces, including stainless steel and plastic, without losing infectivity. Prions bound to metal seem to be highly resistant to decontamination. Few effective decontamination techniques have been published. A 1-2 N sodium hydroxide solution, or a sodium hypochlorite solution containing 2% available chlorine, has traditionally been recommended for equipment and surfaces. Surfaces should be treated for more than 1 hour at 20°C (68°F). Overnight disinfection is recommended for equipment. Cleaning before disinfection removes organic material that may protect prions. Recently, milder

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treatments including a phenolic disinfectant, an alkaline cleaner (KOH with detergents), and an enzymatic cleaner combined with vaporized hydrogen peroxide have been shown to inactivate scrapie prions. The alkaline cleaner and phenolic disinfectant were also effective against BSE and vCJD prions. These disinfectants may be useful for items that cannot withstand harsher decontamination procedures. Physical inactivation of prions can be carried out by porous load autoclaving at 134-138°C (273-280°F) for 18 minutes at 30 lb/in². Autoclaving items in water is more effective than autoclaving without immersion. Dry heat is less effective; hamster-adapted scrapie prions can survive dry heat at temperatures as high as 360°C (680°F) for an hour. A combination of chemical and physical decontamination can be more effective than either procedure alone; chemical disinfection should be carried out first, then the items should be rinsed and autoclaved. Anecdotal evidence suggests that decontamination of contaminated facilities is very difficult.

Even the harshest combination of chemical and physical disinfection is not guaranteed to destroy all prions. In experiments, a stainless-steel wire remained infectious after cleaning with sodium hydroxide and autoclaving. Surgical instruments that have undergone repeated cycles of cleaning and disinfection have transmitted the sporadic (genetic) form of CJD iatrogenically. For this reason, disposable equipment and instruments may be recommended instead of disinfection during some medical procedures.

Infections in Humans

Incubation Period

The incubation period for vCJD is difficult to establish with certainty; however, the average incubation period is estimated to be 11 to 12 years, and incubation periods up to 16 years have been reported. In three cases transmitted in blood transfusions, the incubation period was 6 to 8.5 years. For comparison, some other human prion diseases have similar median incubation periods, but have been reported up to 40 years after exposure.

Clinical Signs

The symptoms of vCJD are broadly similar to the sporadic (genetic) form of CJD, but usually appear in younger patients. The median age of onset is 26 years (range 12–74 years). The first signs are usually psychiatric symptoms such as anxiety, depression, insomnia and social withdrawal, and/or persistent painful sensory symptoms. In most patients, frank neurological signs such as gait disturbances, ataxia, incoordination, memory loss, slurring of speech and tremor appear a few months later; however, neurological signs coincide with or precede psychiatric symptoms in a minority of patients. Cognitive function gradually deteriorates. Chorea, dystonia, myoclonus, visual disturbances and dementia

typically develop late in the course of disease. Most patients die in six months to two years.

Communicability

Person to person transmission of vCJD does not occur during casual contact. Probable human-to-human spread has been reported in several patients who received blood transfusions from asymptotically infected individuals. Other iatrogenic routes of transmission may be possible, including transmission in transplants or by contaminated equipment during surgeries. In humans, prions can be found in the CNS and many lymphoid tissues including the tonsils. Prions have been found in the appendix as early as two years before the onset of clinical disease.

Diagnostic Tests

A tentative diagnosis can be made before death by the history, clinical signs and cortical atrophy on magnetic resonance imaging (MRI) of the brain. The electroencephalogram (EEG) is sometimes normal during the early stages of disease, but later develops characteristic abnormalities. A definitive diagnosis can be made if the abnormal prion protein is found in tonsil biopsies by immunoblot (Western blot) or immunohistochemistry. In other cases, it is made by microscopic examination of brain tissue, usually at necropsy. Numerous amyloid plaques surrounded by vacuoles are found; such plaques are seen in only 5-10% of cases of sporadic (genetic) CJD. Large amounts of prion protein can be found around the plaques by immunohistochemistry.

Treatment

No treatment is available, other than supportive therapy.

Prevention

Variant Creutzfeldt-Jakob disease can usually be avoided by not eating tissues from BSE-infected cattle. Some nations conduct active surveillance of cattle at slaughter (using rapid tests) to detect cases of BSE. In most E.U. nations, all cattle over 30 months of age are tested for BSE if they are destined for human consumption. Fallen stock and emergency slaughter cattle over 24 months of age are also tested. In the E.U. and Japan, a carcass cannot be used in human food until a rapid test is negative. Recently, some countries have extended BSE surveillance to small ruminants. Some countries with a low incidence of disease, including the U.S., test only a percentage of cattle at slaughter. In the U.S., surveillance is targeted particularly at high risk cattle such as nonambulatory animals and those with neurological disease. These animals cannot be used in human food, and the carcass is held until testing is complete.

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Tissues that have a high risk of transmitting BSE have been banned from human food in many countries. In the U.S., prohibited tissues include the brain, skull, eyes, trigeminal ganglia, dorsal root ganglia, spinal cord and most of the vertebrae from cattle 30 months of age and older. The tonsils and distal ileum from all cattle are also banned. In the E.U., banned tissues include the skull and spinal cord in cattle over 12 months of age, and the spinal column in cattle over 24 months of age. The tonsils, intestines and mesentery are not allowed from any cattle. Slaughter and processing techniques that have a high risk of contaminating muscle tissues with CNS have been prohibited in many countries, including the U.S.

Person-to-person transmission of vCJD can be reduced by the use of disposable surgical instruments in high risk surgeries, when this disease is suspected. Because prions can be found in the tonsils, some authors suggest the use of disposable equipment during tonsillectomies in all patients, in countries with a significant risk of this disease. Transmission in blood cannot be completely prevented with current techniques; however, many countries do not allow people who have spent time in the U.K. and/or other European countries to be blood donors. Other measures, such as universal leucodepletion of blood, have also been taken in some countries. In animal studies, blood cells carried a higher risk of transmission than plasma.

Although laboratory or abattoir-related cases have not been reported, veterinarians and laboratory workers should always take precautions when conducting necropsies on BSE-suspects or handling tissues; BSL-3 is the recommended level of protection. Standard precautions include the use of protective clothing, and the avoidance of penetrating injuries, contamination of abraded skin, and ingestion. A negative pressure laminar flow hood should be used for tissue manipulations whenever possible. Because prions may be able to survive in the environment for years and are difficult to disinfect, precautions should be taken to avoid contamination of surfaces and equipment. Disposable plastic-coated paper sheets can be used to protect tables and other surfaces. Disposable instruments and work clothing can also be used. No vaccine is available.

Morbidity and Mortality

The prevalence of vCJD is unknown. Most cases have been seen in people who lived in either the U.K. or France during the peak of the BSE epidemic. As of August 2007, 166 cases of vCJD have been reported in the U.K. The incidence peaked in 2000, when 28 cases were diagnosed, and gradually fell to five cases per year in 2005 and 2006. As of November 2006, an additional 21 cases had been reported from France, as well as four from Ireland, three from the United States and two from the Netherlands. Canada, Italy, Japan, Portugal, Saudi Arabia and Spain have each reported one case. To date, all cases of vCJD in the U.S. seem to have been acquired in other

countries. The number of people who are infected but asymptomatic is unknown. Based on the pattern of infection in the U.K, some sources suggest that, at most, 70 additional cases can be expected. However, surveillance conducted on appendectomy samples in the U.K. suggested a prevalence of 237 cases per million population, with 95% confidence intervals of 49-692.

Variant Creutzfeldt–Jakob disease is usually seen in young patients; the reason for this is unknown. The median age of onset is 26 years for vCJD (range 12–74 years); in the sporadic (genetic) form of Creutzfeldt–Jakob disease, it is 65 years (range 15–94 years). People who are homozygous for methionine at codon 129 in the PrP^C protein have an increased risk of developing vCJD. All clinical cases have occurred in people with this genotype. One infection was reported in a person who was heterozygous for methionine/valine at this codon, but did not develop vCJD symptoms. This person became infected in a blood transfusion and died of unrelated causes after five years. It is not known whether people with resistant genotypes (valine/valine or methionine/ valine) are completely resistant to the development of disease, or simply have a longer incubation period. Once the symptoms of vCJD develop, this disease is always fatal.

Infections in Animals

Species Affected

BSE mainly occurs in cattle. However, the host range of this prion is unusually broad compared to most prions. BSE has been reported from exotic ruminants in zoos; affected species include nyala (*Tragelaphus angasi*), kudu (*Tragelaphus strepsiceros*), gemsbok (*Oryx gazella*), eland (*Taurotragus oryx*), Arabian oryx (*Oryx leucoryx*), scimitar-horned oryx (*Oryx dammah*), ankole cattle and bison (*Bison bison*). Field cases have been documented in two goats, and experimental infections have been reported in both sheep and goats. BSE prions have also caused disease in various felids including housecats, cheetahs (*Acinonyx jubatus*), pumas (*Felis concolor*), ocelots (*Felis pardalis*), tigers (*Panthera tigris*) and Asian golden cats (*Catopuma temminckii*). (See the feline spongiform encephalopathy factsheet for details on infections in felids.) Two lemurs at a French zoo were apparently infected in contaminated feed. In addition, the BSE agent has been experimentally transmitted to mink, mice, marmosets and cynomolgus monkeys. Pigs could be infected by the intracranial, intravenous and intraperitoneal routes, but short-term feeding trials did not cause disease.

Incubation Period

The incubation period is estimated to be 2 to 8 years in cattle. The peak incidence of disease occurs in four to five year old animals.

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The incubation period in experimentally infected sheep varies with the animal's age and genetic susceptibility, and the route of exposure and dose. In genetically susceptible sheep, the incubation period was 21 to 38 months for animals inoculated orally at six months of age, and 18 to 24 months in lambs inoculated orally at two weeks of age. In genetically resistant (ARR/ARR) sheep, the incubation period was approximately 3 to 5 years.

In experimentally infected macaques inoculated orally, the incubation period was 3.6 to 5 years.

Clinical Signs

Bovine spongiform encephalopathy is a neurological disease that usually has an insidious onset in cattle. The symptoms may include gait abnormalities (particularly hindlimb ataxia), hyperresponsiveness to stimuli, tremors, and behavioral changes such as aggression, nervousness or apprehension, changes in temperament and even frenzy. The combination of behavioral changes, hyperreactivity to stimuli and gait abnormalities is highly suggestive of BSE, but some animals exhibit only one category of neurological signs. Pacing, a modified gait in which the legs move in lateral pairs, occurred in 25% of the cattle with BSE in one study, and may be suggestive of this disease. Intense pruritus is not usually seen, but some animals may lick or rub persistently. Nonspecific symptoms include loss of condition, weight loss, teeth grinding (possibly due to visceral pain or neurological disease) and decreased milk production. Decreased rumination, bradycardia and altered heart rhythms have also been reported. The symptoms of BSE usually worsen gradually over a few weeks to six months, but rare cases can develop acutely and progress rapidly. Rapid, acute-onset neurological disease seems to be particularly common in exotic ruminants in zoos. Once the symptoms appear, BSE is always progressive and fatal. The final stages are characterized by recumbency, coma and death.

Little is known about the features of atypical BSE in cattle. Although neurological disease has been reported, very few cases have had the classical combination of behavioral disturbances, sensory signs and gait abnormalities. Some atypical strains have been found in asymptomatic cattle during routine surveillance.

Various neurological symptoms have been reported in experimentally infected sheep. In one study, Cheviot sheep mainly developed ataxia with minimal pruritus, and died in a few days to a week. In indigenous French breeds, the symptoms included ataxia and intense pruritus with loss of fleece. These animals deteriorated slowly and died in approximately three months. The BSE cases in naturally infected goats were discovered during routine surveillance at slaughter.

Post Mortem Lesions [Click to view images](#)

Gross lesions are not found in BSE, with the exception of nonspecific signs such as emaciation or

wasting. The histopathologic lesions are confined to the CNS. Neuronal vacuolation and non-inflammatory spongiform changes in the gray matter are characteristic of the disease in cattle. These lesions are usually but not always bilaterally symmetrical. Amyloid plaques are not typical of classical BSE, but are associated with atypical L-form BSE prions.

Similar spongiform changes occur in experimentally infected sheep and macaques.

Communicability

There is little or no evidence that the BSE agent is transmitted horizontally between cattle, but the offspring of infected animals have an increased risk of developing this disease. The route of transmission is unknown.

Diagnostic Tests

There is no live animal test for BSE. This disease is usually diagnosed by detecting prions (PrP^{res}) in the CNS. Accumulations of prions can be found in unfixed brain extracts by immunoblotting, and in fixed brains by immunohistochemistry. In addition, several rapid diagnostic tests based on enzyme-linked immunosorbent assays (ELISAs) and automated immunoblotting (Western blotting) are available. Rapid tests allow large numbers of samples to be screened and are often used in surveillance and slaughter testing. Positive samples in rapid tests are confirmed with more specific assays such as immunohistochemistry or immunoblotting. A diagnosis of BSE may also be confirmed by finding characteristic prion fibrils called scrapie-associated fibrils (SAF) with electron microscopy in brain extracts. Some of these tests can be used on frozen or autolyzed brains. Techniques to detect prions are relatively insensitive compared to assays for other types of pathogens; prions cannot usually be detected in the brain until 3-6 months before the onset of disease. Atypical BSE prions can be detected by some assays, and have a somewhat different distribution in the brain than classical BSE prions.

Histological examination of the brain is also very helpful in diagnosis, but some animals in early stages of infection have few or no spongiform changes. In addition, BSE can be detected by transmission studies in mice. However, an incubation period of several months often makes this technique impractical for routine diagnosis. Serology is not useful for diagnosis, as antibodies are not made against the BSE agent.

Treatment

There is no treatment for BSE. Suspect animals are usually euthanized for testing.

Prevention

BSE can be prevented by not feeding ruminant tissues that may contain prions to susceptible species. Complete avoidance is generally necessary, as cooking or rendering cannot completely inactivate prions. Many nations have

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now banned the use of either ruminant or mammalian proteins, with certain exceptions such as milk and blood, in livestock feed. This measure can interrupt transmission of the agent and control BSE epidemics; however, due to the long incubation period, the number of BSE cases may not decline for some time. In addition, countries may place trade bans on the importation of live cattle and certain ruminant proteins from affected countries.

BSE suspects are usually euthanized for testing. These carcasses cannot be used as food and must be destroyed. In the U.K., BSE carcasses are rendered at 133°C (3 bar pressure) for at least 20 minutes. Surveillance can help prevent infected animals from being used in food. Some nations conduct active surveillance of cattle at slaughter (using rapid tests) to detect cases of BSE. In most E.U. nations, all cattle over 30 months of age are tested for BSE if they are destined for human consumption. Fallen stock and emergency slaughter cattle over 24 months of age are also tested. In the E.U. and Japan, a carcass cannot be used in human food until a rapid test is negative. Recently, some countries have extended BSE surveillance to small ruminants.

Some countries with a low incidence of disease, including the U.S., test only a percentage of cattle at slaughter. In the U.S., surveillance is targeted particularly at high risk cattle such as nonambulatory animals and those with neurological disease. These animals cannot be used in human food, and the carcass is held until testing is complete. The U.S. also conducts passive surveillance for BSE. When an infected animal is identified, the affected herd is quarantined, and the source of the infection is investigated. Due to the increased risk of BSE in the offspring of infected cattle, they are usually traced and euthanized.

Tissues that have a high risk of transmitting BSE have been banned from human food in many countries. In the U.S., prohibited tissues include the brain, skull, eyes, trigeminal ganglia, dorsal root ganglia, spinal cord and most of the vertebrae from cattle 30 months of age and older. The tonsils and distal ileum from all cattle are also banned. In the E.U., banned tissues include the skull and spinal cord in cattle over 12 months of age, and the spinal column in cattle over 24 months of age. The tonsils, intestines and mesentery are not allowed from any cattle. Slaughter and processing techniques that have a high risk of contaminating muscle tissues with CNS have been prohibited in many countries, including the U.S.

Morbidity and Mortality

BSE is seen most often in four to five year old cattle, particularly dairy animals. This disease is always fatal once the symptoms appear. The prevalence of BSE varies widely. In some countries, the estimated prevalence may be more than 100 cases per million cattle, in others, there may be fewer than two cases per million. The latter are defined as World Organization for Animal Health (OIE) 'minimal risk' countries for BSE.

BSE epidemics have been reported in several European countries. The first outbreak occurred in the U.K., where more than 180,000 cases have been confirmed since the 1980s. The U.K. epidemic peaked in 1992, with nearly 1,000 new cases confirmed each week. At the time, the annual incidence in affected herds was approximately 2-3%. As a result of control measures (particularly feed bans), the incidence declined to approximately 5-10 new cases per week in 2004. The peak of the epidemic curve occurred later in countries where feed bans were established more recently. In the U.S., only three cases of BSE have been reported. One case occurred in an animal imported from Canada. Two additional cases have been reported in indigenous cattle; one was caused by the H-form of atypical BSE.

Little is currently known about the incidence of atypical BSE. Some studies suggest that up to 5-10% of the animals diagnosed with rapid screening tests might be infected with atypical BSE prions, but this is based on very limited data.

As of August 2007, only two cases of BSE have been reported in goats. Infections have not been seen in sheep other than experimentally infected animals. Surveillance conducted in Europe suggests that the prevalence of BSE is very low in this species, if it occurs at all. Estimates of the maximum proportion of sheep TSE cases that could be BSE range from 0.7% to 5%. Experimentally infected sheep that are genetically resistant to scrapie seem to have some resistance to BSE, but are not immune to infection or disease.

Internet Resources

Canadian Food Inspection Agency

<http://www.inspection.gc.ca/english/anima/heasan/disemala/bseesb/bseesbindexe.shtml>

Centers for Disease Control and Prevention

<http://www.cdc.gov/ncidod/dvrd/bse/index.htm>

European Commission. BSE / Scrapie

http://ec.europa.eu/food/food/biosafety/bse/index_en.htm

Manual for the Recognition of Exotic Diseases of Livestock

<http://www.spc.int/rahs/>

The Merck Veterinary Manual

<http://www.merckvetmanual.com/mvm/index.jsp>

The National Creutzfeldt-Jakob Disease Surveillance Unit, United Kingdom.

<http://www.cjd.ed.ac.uk/index.htm>

United Kingdom. Department for Environment Food and Rural Affairs. Bovine Spongiform Encephalopathy

<http://www.defra.gov.uk/animalh/bse/index.html>

United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service. Bovine Spongiform Encephalopathy

http://www.aphis.usda.gov/newsroom/hot_issues/bse/index.shtml

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USDA Foreign Agricultural Service. Bovine Spongiform Encephalopathy
<http://www.fas.usda.gov/DLP/BSE/bse.html>

United States Food and Drug Administration. Bovine Spongiform Encephalopathy
<http://www.fda.gov/oc/opacom/hottopics/bse.html>

World Health Organization. Bovine Spongiform Encephalopathy
<http://www.who.int/mediacentre/factsheets/fs113/en/>

World Organization for Animal Health (OIE)
<http://www.oie.int>

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/eng/normes/mmanual/a_summry.htm

OIE Terrestrial Animal Health Code
http://www.oie.int/eng/normes/mcode/A_summry.htm

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