Transmissible Spongiform Encephalopathies of Animals

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Importance

Transmissible spongiform encephalopathies (TSEs) are neurodegenerative diseases caused by prions. Although these infections usually remain asymptomatic for years, the disease is always progressive and fatal once the clinical signs develop. TSEs affecting animals include scrapie (tremblante de mouton, rida), bovine spongiform encephalopathy (BSE, "mad cow disease"), feline spongiform encephalopathy (FSE), transmissible mink encephalopathy (TME, mink scrapie) and chronic wasting disease (CWD). Although some prion diseases usually occur in one or a few closely related species, other prions can cross species barriers. BSE has a particularly wide host range. Cattle are the primary hosts for this disease, but some other ruminants, cats, lemurs and humans can also be affected; in cats, the disease is known as feline spongiform encephalopathy and in humans, it is called variant Creutzfeldt-Jakob disease (vCJD). Some evidence also suggests that TME might be a caused by an atypical variant of the BSE agent called L-BSE. The discovery that BSE can cross species barriers and is zoonotic has raised concerns about all TSEs. Prion diseases in livestock can also result in trade sanctions. For these reasons, many countries are conducting control or eradication programs.

This document contains general information about the various prion diseases found in animals. Additional details can be found in the individual factsheet for each disease.

Etiology

Transmissible spongiform encephalopathies are caused by prions, 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} ('res' refers to the proteinase K-resistant nature of prions, compared to normal PrPc). Alternative names for this protein are PrP^{TSE}, PrP^{Sc} ('Sc' stands for scrapie, the first animal prion disease to be recognized) and PrP^{d} (for disease-associated). Different prions (or, more accurately, different strains of PrP^{res}) cause scrapie, bovine spongiform encephalopathy (BSE) and chronic wasting disease (CWD). BSE in felids is called feline spongiform encephalopathy (FSE), and BSE in zoo ruminants was formerly called 'spongiform encephalopathy of exotic ruminants.'

There are both classical and atypical BSE and scrapie prions. Atypical prions were first recognized during the last 20 years, as the result of enhanced surveillance for TSEs. The term 'classical' is used to distinguish the usual BSE and scrapie strains from these newly recognized forms. There are at least two atypical BSE prions. One has higher molecular mass fragments than classical BSE in an immunoblot and is called H-type BSE or H-BSE; the other has a lower molecular mass and is called L-type BSE or L-BSE. Currently, the most likely hypothesis is that L-BSE and H-BSE arise spontaneously in cattle, as genetic diseases. One of them may have given rise to the classical BSE epidemic after amplification through the food chain. Atypical/ Nor98 scrapie might, similarly, be a spontaneously occurring prion disease of small ruminants; however, this is not yet certain.

Which prion causes transmissible mink encephalopathy (TME) is still uncertain; however, it is expected to be an agent that occurs in meat fed to ranched mink. Current evidence suggests that it may be atypical L-BSE, although other possibilities, such as certain strains of the scrapie prion, have not been entirely ruled out.

Species Affected

Most prions seem to occur naturally in a small number of related species. Scrapie can affect sheep, goats, mouflon (*Ovis musimon*), and possibly other animals closely related to sheep and goats. Atypical/Nor98 scrapie has been found in both sheep and goats. CWD appears to be limited to cervids. As of 2016, it has been reported in free-living and/or captive mule deer (*Odocoileus hemionus*), black-tailed deer (*O. hemionus columbianus*), white-tailed deer (*O. virginianus*), Rocky Mountain elk (*Cervus elaphus nelsoni*), red deer (*C. elaphus elaphus*), sika deer (*C. nippon*), moose (*Alces alces*) and reindeer (*Rangifer tarandus tarandus*). TME has been seen only in ranched mink (*Neovision (Mustela) vision)*. In contrast, the host range of the classical BSE prion

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seems to be unusually broad. While cattle are the primary hosts, this prion has been found in housecats and captive zoo felids (where it is known as FSE), various species of exotic ruminants in zoos, two lemurs in a French zoo, and at least two goats. H-BSE and L-BSE have only been detected in cattle, to date, although some researchers suspect that L-BSE might cause TME in mink.

Some prions have been transmitted experimentally to additional species by routes that could occur in nature. Animals infected by feeding BSE prions include sheep, mink, cynomolgus macaques (*Macaca fascicularis*) and European red deer, but not pigs. Red deer did not appear to be very susceptible: only one of 6 animals became infected after they were fed a high dose of prions. Lemurs could be infected with L-BSE by the oral route, but little is otherwise known about animals' susceptibility to H-BSE or L-BSE. Scrapie does not seem to be transmitted readily to animals other than small ruminants. Squirrel monkeys (*Saimiri sciureus*) became infected when they were fed tissues that contained hamster-adapted scrapie prions, but several other species of primates, cattle and pigs did not appear to be susceptible. One fish (sea bream, *Sparus aurata*) had evidence of infection after oral inoculation with either BSE or scrapie prions. CWD can infect additional cervids and squirrel monkeys by the oral route, but attempts to infect cattle, cats, ferrets, mink and cynomolgus macaques have failed. Epidemiological studies also suggest that cattle are unlikely to be susceptible to this agent. Studies to date have found no evidence of CWD in wild predators and scavengers, such as coyotes (*Canis latrans*), mink, opossums (*Didelphis virginiana*) and raccoons (*Procyon lotor*), in endemic areas. There are few published experiments with TME; however, raccoons can be infected by either oral or parenteral routes.

Most prions have been transmitted to various animals other than their natural hosts by intracerebral inoculation. Because this route bypasses normal species barriers, it does not necessarily indicate that a species would be susceptible to that prion in nature. However, the absence of replication suggests it is unlikely to be susceptible. For instance, cats were resistant to scrapie via intracerebral inoculation, and CWD could not be transmitted to cynomolgus macaques or raccoons.

Zoonotic potential

Humans occasionally develop variant Creutzfeldt-Jakob disease (vCJD) after eating prion-containing tissues from an infected animal. To date, all known cases have been caused by the classical BSE prion, and the zoonotic potential of H-BSE and L-BSE is unclear. While FSE is also caused by the classical BSE prion, no cases of vCJD appear to have been acquired from cats. There is one curious case, where spongiform encephalopathies were reported simultaneously in a cat and its owner in 1998, and the prions found in both man and cat appeared to be similar. However, these prions differed from BSE, and the man was subsequently found to have the sporadic form of Creutzfeldt-Jakob disease, which is thought to be a spontaneous genetic disease.

As of 2016, investigations of suspicious cases of neurological disease in humans, surveillance, and epidemiological studies have found no evidence that CWD can affect humans. Nevertheless, the possibility that this agent is zoonotic cannot be ruled out at this time. People are not thought to be susceptible to scrapie, a disease that has been known since the 18th century.

Geographic Distribution

Animal prion diseases resemble neurological diseases caused by other agents, and information about their distribution can be incomplete outside regions with good veterinary surveillance. Classical scrapie has been reported on all major continents and some islands, although some countries recently found few or no cases during active surveillance. Australia and New Zealand have remained scrapie-free, with the exception of an outbreak caused by imported animals in the 1950s. Cases of classical BSE have been reported in indigenous cattle in some European countries, Canada, Israel and Japan. Some of these countries may have eradicated BSE, as it has not been detected in some time. Some other nations, including the U.S., have found this agent only in imported cattle. FSE has been reported in some countries where BSE occurs, and in housecats or zoo cats imported from these countries. Most infected animals had lived in the U.K. during the BSE epidemic.

Atypical BSE prions and atypical/ Nor98 scrapie prions have been reported in Europe, North America (both Canada and the U.S.) and some other countries, as the result of surveillance programs for TSEs. Both of these prions have been found in countries that are free of the classical form of that disease. Their presence does not affect a nation's scrapie or BSE status for international trade.

CWD has been found mainly in North America. It has been spreading from its original, limited focus in the U.S., and now occurs in a number of U.S. states and parts of Canada. This disease was imported to the Republic of Korea in captive cervids in 2001, and has been found there in captive animals, most recently in 2010. In 2016, CWD was detected in wild cervids in Norway. TME has been reported in ranched mink in the U.S., Canada, some European countries and the former U.S.S.R.

Transmission

TSEs are thought to be acquired primarily by ingestion, although some prions may also enter the body by other routes. Prions occur mainly in the central nervous system (CNS) of TSE-infected animals, but they can also be found in lymphoid tissues, peripheral nerves and various organs, to a greater or lesser extent depending on the prion and host species. Animals carry prions for life, and can transmit them even if they remain asymptomatic. Prions have also been transmitted iatrogenically in some species (e.g., via contaminated surgical instruments or in blood transfusions).

BSE, FSE and TME do not seem to be transmitted horizontally between animals. Animals (including cats with FSE) become infected with classical BSE prions when they

eat contaminated tissues from infected animals. BSE prions caused epidemics in cattle when they were amplified by recycling tissues from infected cattle into ruminant feed supplements. Young animals appear to be infected more readily than cattle over the age of 6 months. Vertical transmission has been reported in experimentally infected sheep, but it has not been documented in cattle. However, the offspring of BSE-infected cows seem to have an elevated risk of developing BSE, for reasons that are still unclear. There is one report of possible maternal transmission of FSE in a cheetah. TME is, likewise, thought to spread primarily by ingestion, probably when mink are fed tissues from infected animals; however, some evidence suggests that this prion might also enter the body through breaks in the mucous membranes or skin. Vertical transmission does not seem to occur in mink.

Scrapie and CWD can be transmitted directly between animals, or indirectly via the environment. CWD prions have been found, though sometimes at very low levels, in the saliva, blood, urine, feces and antler velvet of cervids. Most animals are thought to acquire this disease from the environment, probably during grazing. Vertical transmission has been documented in some cervid species. Most small ruminants seem to acquire scrapie from their dam during the neonatal period, although they can also become infected from unrelated animals or the environment. Older animals remain susceptible, though to a lesser extent. The placenta can contain scrapie prions, with particularly large amounts in sheep, and newborns may be infected by licking fetal membranes and fluids. The milk and colostrum of small ruminants are also infectious. *In utero* infection appears possible in sheep, though rare. Highly sensitive techniques have found low levels of scrapie prions in the urine, saliva and feces of sheep, but how much these sources contribute to transmission is still uncertain. The epidemiology of atypical/Nor98 scrapie suggests that it is not transmitted efficiently (or perhaps at all) between animals in nature, although laboratory experiments have demonstrated that newborn lambs are susceptible to oral inoculation.

Prions can persist for long periods in the environment. Infectious scrapie and CWD prions have been found in soil for 1.5 to 3 years or more in laboratory experiments. Evidence from Iceland, where scrapie-affected premises are not restocked for at least 2 years after depopulation and decontamination, suggests that this prion can infect animals up to 16 years later, under some conditions. Soil-bound prions remain infectious for animals. Repeated cycles of wetting and drying are reported to decrease, though not necessarily eliminate, soil infectivity. Prions can also remain infectious after passage through the digestive tracts of mammals and birds that eat infected animals.

Zoonotic transmission

In humans, variant Creutzfeldt-Jakob disease usually results from the ingestion of BSE prions, but a few people have been infected in blood transfusions from asymptomatic individuals. Other potential routes of infection include organ/tissue transplantation and surgical transmission via contaminated equipment. Prions do not spread between people during casual contact.

Disinfection

Complete decontamination of prion-contaminated tissues, surfaces and environments can be difficult. These agents are very resistant to most disinfectants, including formalin and alcohol. They are also resistant to heat, or ultraviolet, microwave 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.

Relatively few prion decontamination techniques have been published and confirmed to be effective for routine use. Some laboratories pre-treat tissues with formic acid to decrease infectivity before sectioning tissue blocks. A 1-2 N sodium hydroxide solution, or a sodium hypochlorite solution containing at least 2% (20,000 ppm) 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. Experimentally, some milder treatments have also been effective against certain prions, under some conditions. They include a specific phenolic disinfectant, various alkaline and enzymatic detergents (although the efficacy of specific agents within these classes varies), hydrogen peroxide gas plasma, radiofrequency gas plasma, and sodium dodecyl sulfate plus acetic acid. These agents might be useful for items that cannot withstand harsher decontamination procedures.

Physical inactivation of prions can be carried out by porous load autoclaving at 134°C (273°F) for 18 minutes at 30 lb/in^2. Resistance to heat may vary with the specific prion, the degree of contamination and type of sample. Tissue films containing prions are more difficult to decontaminate by steam after they have dried, and human guidelines for surgical instruments recommend that, after use, they be kept moist or wet until decontamination is performed. The cleaning agent used before autoclaving should also be chosen with care, as certain agents (e.g., some enzymatic treatments) can increase the resistance of prions to steam sterilization. Dry heat is less effective than moist heat; some prions can survive dry heat at temperatures as high as 360°C (680°F) for an hour, and one group even reported that infectivity survived incineration at 600°C (1112°F). A combination of chemical and physical decontamination can be more effective than either procedure alone, and effective combinations of chemical agents (e.g., NaOH) and autoclaving have been published. It should be noted that even the harshest combination of chemical and physical disinfection is not guaranteed to destroy all prions in all types of samples.

Decontaminating contaminated facilities, especially sites such as animal pens, may be very difficult. In one study, genetically susceptible sheep became infected with scrapie after being placed in pens that had been pressure washed and decontaminated with high concentrations of sodium hypochlorite (20,000 ppm free chorine solution) for one hour, followed by painting and full re-galvanization or replacement of metalwork. Decontaminating soil contaminated with prions is currently impractical, although some agents, including an aqueous subtilisin-based enzymatic treatment (effective at ambient temperatures), appear promising in the laboratory. Incineration is commonly used for carcasses, but two studies found that composting may reduce or eliminate scrapie and other prions in tissues, while another suggested that soil microorganisms might degrade prions in buried carcasses.

Infections in Animals

Incubation Period

Transmissible spongiform encephalopathies have incubation periods of months or years. TME has the shortest estimated incubation period, at 6-12 months, while scrapie, BSE, FSE and CWD usually become apparent after 2 years or more in their natural hosts. Clinical cases can occur before this time, but are uncommon.

Clinical Signs

Transmissible spongiform encephalopathies are usually insidious in onset and tend to progress slowly. In most of these diseases, the clinical signs primarily involve the nervous system, and often include changes in behavior, as well as frank neurological signs such as tremors, ataxia and hyperreactivity to stimuli. Intense pruritus is common in sheep with classical scrape; however, it tends to be less severe or absent in goats with this disease, and it is minimal or uncommon in most sheep or goats infected with atypical scrapie prions. Pruritus is not a common sign in BSE, CWD or TME. Loss of condition can be seen with all TSEs; however, wasting is particularly prominent in cervids with CWD, and some animals become severely emaciated before they die. Some cervids present mainly with weight loss, and few or subtle neurological signs. Once an animal becomes symptomatic, all TSEs are relentlessly progressive and fatal, typically within weeks to months.

Post Mortem Lesions

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There are no pathognomonic gross lesions in TSE-infected animals, although non-specific lesions may be seen. Animals that die or are euthanized in the early stages of these diseases may be in good condition; however, loss of condition is common later, and wasting of the carcass is often prominent in cervids with CWD. CWD can also result in megaesophagus and aspiration bronchopneumonia (which may be the cause of death), and classical scrapie-infected animals may have evidence of pruritus.

The typical histopathological lesions of TSEs are confined to the CNS. These lesions are usually (though not always) bilaterally symmetrical, and are characterized by non-inflammatory spongiform changes, with neuronal vacuolation and varying degrees of astrocytosis. Amyloid plaques may be seen in L-BSE and some cases of scrapie or CWD, but they are not usually found in other prion diseases, including classical BSE and H-BSE.

Diagnostic Tests

All TSEs can be diagnosed by examining the brain for prions at necropsy. In most diseases, prions can be detected in the medulla oblongata at the level of the obex; however, atypical/Nor98 scrapie can be missed by sampling only this site, and is more likely to be found in the cerebellum and other CNS locations. Asymptomatic ruminants can be tested for BSE or scrapie at routine slaughter by sampling the brainstem through the foramen magnum. TSEs may also be detected in lymphoid tissues at necropsy; in particular, scrapie and CWD can sometimes be found in these tissues before they are detected in the brain, and before the clinical signs appear.

Classical scrapie and CWD can also be diagnosed in live animals with biopsies of lymphoid tissues. Standardized sampling sites include the rectoanal mucosa-associated lymphoid tissue and palatine tonsil in both diseases, and the nictitating membrane (third eyelid) in scrapie. Rectal mucosa and nictitating membrane biopsies can be taken without sedation, using only topical anesthesia and restraint, and are more practical than tonsil biopsies in the field. Prions may occasionally be found in other lymphoid tissues, such as superficial lymph nodes. Live animal tests do not appear to be capable of detecting animals with atypical/Nor98 scrapie.

Immunoblotting (Western blotting) or immuno-histochemistry are the most specific assays for detecting prions, and can be used in all of the animal prion diseases. A number of rapid diagnostic tests based on enzyme-linked immunosorbent assays (ELISAs), automated immunoblotting or other techniques (e.g., lateral flow assays) have also be validated for BSE and classical scrapie. Some of these tests appear to be capable of detecting other TSEs, though with varying efficacy. Rapid tests allow large numbers of samples to be screened, and are often used in surveillance and slaughter testing. Histological examination of the brain can be very helpful in the diagnosis of prion diseases (although it is not generally used as the sole confirmatory test), but some animals in the early stages of infection have few or no spongiform changes. The presence of characteristic prion fibrils in the brain, called scrapie-associated fibrils (SAF), may be used to diagnose TSEs with electron microscopy, even in autolyzed brains; however, this test has low sensitivity.

Highly sensitive assays, including protein misfolding cyclic amplification (PMCA) and quaking-induced conversion (QuIC) or real-time quaking-induced conversion (RT-QuIC), may be able to identify infected animals earlier than immunoblotting or immunohistochemistry. They can also find prions in tissues where they are present in very low

amounts. These techniques detect tiny amounts of prions by their ability to convert PrP^c (the normal cellular protein) into prions *in vitro*. They are mainly used in research at present, but are being investigated for possible diagnostic use in several diseases. TSEs can also be detected by inoculation into mice (rodent bioassays); however, an incubation period of several months makes this technique impractical for routine diagnosis. Serology is not useful for diagnosis, as antibodies are not made against prions.

Treatment

There is no treatment for any prion disease.

Control

Disease reporting

Veterinarians who encounter or suspect a prion disease should follow their national and/or local guidelines for disease reporting. Diseases that are absent from a nation are reportable immediately in most countries. Endemic diseases can also be reportable, although the requirements may be different.

In the U.S., state or federal veterinary authorities should be informed immediately of any cases of BSE, FSE or TME. The U.S. has an eradication program for scrapie, and this disease is also reportable. Requirements for CWD may vary with the state, and with a farmed cervid herd's participation in the U.S. herd certification program. Local wildlife management agencies are often responsible for CWD surveillance programs in wild cervids.

Prevention

BSE, FSE and TME can be prevented by not feeding tissues that may contain prions to susceptible species. Complete avoidance is necessary, as cooking or rendering cannot completely inactivate these agents. Banning ruminant (or mammalian) tissues from ruminant (or animal) feed has significantly reduced the number of new cases of BSE and controlled the epidemics in cattle. The specific bans, and protein sources prohibited, vary with the country. Surveillance and tracing of infected animals can reveal cohorts that may have received the same feed. Countries may place trade bans on the importation of live animals and certain animal proteins from TSE-affected nations.

Diseases that can spread horizontally, such as scrapie and CWD, require additional methods of control. The risk of introducing these diseases can be reduced by maintaining a closed herd/ flock or minimizing outside purchases of stock. If replacement animals must be added, they should be from herds that test negative for the disease and are managed in a way that makes them unlikely to become infected. Milk and colostrum from potentially infected sheep or goats should not be fed to scrapie-free flocks. Reducing exposure to high concentrations of prions (e.g., in the placenta of sheep) may reduce transmission within a herd or flock that has become infected. The risk that a sheep will develop scrapie is strongly influenced by its genotype, and selecting genetically resistant animals can aid control efforts. Whether genetic control methods are feasible in scrapie-infected goat herds or CWD-infected cervid herds is still uncertain. Complete depopulation, followed by cleaning and disinfection, is sometimes used on prion-infected farms; however, decontamination may be difficult and the disease may recur. Some countries have developed voluntary and/or mandatory programs to control CWD and scrapie, with eradication from domestic herds/ flocks as the ultimate goal.

Controlling CWD in wild cervids is very difficult. Infected captive cervids should be kept from contact with wild cervids, to avoid transmitting this disease to uninfected areas. Many states and provinces also have restrictions on transporting tissues from hunter-killed cervids in CWD-endemic areas. Attempts to reduce transmission in wild populations include banning practices that encourage cervids to congregate in certain areas (e.g., feeding or baiting), and culling to reduce animal densities. Other TSEs are not known to be an issue in wild animals.

There are no established control methods for L-BSE, H-BSE or atypical/ Nor98 scrapie, which could be spontaneous genetic diseases. These prions do not currently affect a nation's BSE or scrapie status for international trade.

Morbidity and Mortality

TSEs are usually diseases of adult animals. Only adult mink are usually affected by TME; in at least one outbreak, kits housed with their dams and eating the same diet were completely spared. The peak incidence of classical BSE occurs in 4-6 year-old cattle, while classical scrapie peaks in sheep between the ages of 2 and 5 years, and CWD in captive cervids between 2 and 7 years. All of the ruminant and cervid TSEs are very rare or absent in animals that are less than 12-18 months of age. L-BSE, H-BSE and atypical/Nor98 scrapie tend to occur in animals older than those with classical BSE or classical scrapie, respectively. All TSEs are fatal once clinical signs appear.

The animal's genotype influences the onset and severity of some TSEs. This is particularly well-known in sheep, where susceptibility or resistance to classical scrapie is associated with polymorphisms in the PrP gene at codons 136, 154 and 171. Sheep with resistant genotypes become ill after longer incubation periods, or not at all. A genetically resistant fetus also suppresses the appearance of prions in the placenta of its genetically-susceptible, infected dam. The genes that affect scrapie resistance are not as well understood in goats, but some polymorphisms have been identified, and one (K222) has been proposed as a possible target for breeding more scrapie-resistant animals. Atypical scrapie is also affected by the animal's genotype; however, this disease seems to be common in sheep resistant to classical scrapie, and underreported in the animals most susceptible to the latter form. Genetic susceptibility to CWD is not yet well understood.

TSEs vary greatly in prevalence, depending on the country, host species and specific disease. Atypical BSE and atypical scrapie seem to arise sporadically, at low levels, in their respective host species. Atypical scrapie prions are typically found in only a single animal per flock or herd, while

only about 100 animals infected with L-BSE or H-BSE have been identified since surveillance began. TME also seems to be rare, with few reported outbreaks. However, large numbers of mink are often affected on infected ranches. FSE was documented in approximately a hundred housecats and twenty zoo felids between 1990 and 2007. Most of these cases occurred in the U.K. during the BSE epidemic, and new cases have not been published since 2007.

Classical BSE, classical scrapie and CWD can be common in some areas. Most BSE cases occurred during epidemics that began in the 1980s in the U.K., and resulted from recycling tissues from infected animals in ruminant feed. At one time, the estimated prevalence of classical BSE in infected countries ranged from more than 100 cases per million cattle to fewer than 2 cases per million. As a result of control measures (particularly feed bans), the incidence of this disease has declined worldwide. In the U.K., the number of new cases has dropped from nearly 1,000 per week, at the height of the epidemic in 1992, to 0-3 cases per year between 2012 and 2016.

Classical scrapie can be a significant problem in some areas, while other regions report few or no cases. This disease is much less common in goats than sheep. Between 2002 and 2009, surveillance programs in the E.U. identified approximately 3300 infected goats, compared to about 15,000 sheep. The average prevalence of scrapie in sheep was 0.087% in E.U. countries reporting this disease between 2002 and 2012, and 0.015% in the U.S., as of 2013. In North America, the prevalence of CWD in wild cervids is reported to be < 5% in deer and < 2.5% in elk in many affected areas. However, it differs between regions, and can be higher in localized "hot spots," where it may be present in up to 10-12% of elk and up to 50% of wild deer. Only a few CWD cases have been reported, to date, in wild cervids in Norway, and its prevalence there is uncertain.

Infections in Humans

BSE

BSE is the only animal TSE known to affect humans; people who have eaten BSE prions may develop variant Creutzfeldt-Jakob disease. As of May 2016, 228 cases of vCJD have been reported worldwide. With the exception of 27 cases in France, most of these people had resided in the U.K. for more than 6 months during the peak of the BSE epidemic, and are likely to have been infected there. In the U.K., the incidence of vCJD peaked in 2000, when 28 cases were diagnosed, and gradually fell to 2-5 cases per year between 2006 and 2011. Only two additional cases were recognized between 2012 and 2016. The number of people who have been infected asymptomatically, and the percentage of those likely to develop vCJD, is still unclear. Based on the decreasing number of clinical cases, some sources suggest that few additional cases may be seen. However, some studies that have examined lymphoid tissues, such as the tonsils or appendix, suggest that from 1 in 2000 to 1 in 10,000 people in the U.K. may be infected subclinically with BSE prions. Whether these people will ever develop vCJD is not known.

The symptoms of vCJD are broadly similar to the sporadic (genetic) form of Creutzfeldt-Jakob disease, but usually appear in younger patients. The median age of onset is 26 years, although cases have been reported in people from 12 to 74 years. The first signs are usually psychiatric symptoms such as anxiety, depression and social withdrawal, and/or persistent painful sensory symptoms. In most patients, frank neurological signs (e.g., ataxia, tremors) appear a few months later; however, neurological signs coincide with or precede psychiatric symptoms in a minority of patients. Cognitive function gradually deteriorates, and involuntary movements and visual disturbances may develop late in the course of the disease. There is no known treatment, and most patients die within 2 years. To date, all individuals with confirmed clinical cases have been homozygous for methionine at codon 129 in the PrP^{C} protein.

Prevention of vCJD is based on the avoidance of high-risk tissues from cattle. Many countries exclude animals with BSE-like clinical signs, as well as high risk tissues from asymptomatic cattle (specified risk materials or SRM), from human food. SRM generally include the brain, spinal cord, associated bones and some nerve ganglia; tonsils; and various portions of the intestinal tract (e.g., currently, the distal ileum in the U.S., and the last 4 meters of the small intestine, the cecum and mesentery in the E.U.). Some nations conduct active surveillance of cattle at slaughter, using rapid tests, to detect cases of BSE. Positive carcasses are destroyed. Slaughter and processing techniques that have a high risk of contaminating muscle tissues with CNS have also been prohibited in many nations. Many countries restrict blood donations from people with a significant risk of having been infected during the BSE epidemics. Some may also take other measures to prevent transmission in blood transfusions or during high-risk surgical procedures. 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 for handling these prions.

CWD

Although no human infections with CWD have ever been reported, the possibility that this disease could be zoonotic has not been ruled out. Hunters should consider having carcasses tested for CWD; information on this program is available from most state wildlife agencies in the U.S. Meat from cervids that appear to be ill, as well as meat from apparently healthy animals that test positive for CWD, should not be eaten or fed to any animals. Gloves should be worn when field-dressing a cervid carcass. Boning-out the meat and minimizing the handling of the brain, spinal cord and lymphoid tissues associated with the gastrointestinal tract (e.g. tonsils) from cervids may reduce the risk of exposure, but will not necessarily remove all prions.

Internet Resources

Canadian Food Inspection Agency (CFIA). BSE

Canadian Food Inspection Agency. Chronic Wasting Disease (CWD) of Deer and Elk (including information on the herd certification program)

Centers for Disease Control and Prevention (CDC). Prion Diseases.

Chronic Wasting Disease Alliance

European Commission. Control of TSEs (including BSE and scrapie)

European Food Safety Authority. Transmissible Spongiform Encephalopathies

European Union Reference Laboratory, TSE-LAB-NET

Scrapie Canada

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

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

U.K. DEFRA. Exotic species and domestic cats: TSE surveillance statistics

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

USDA APHIS. Chronic Wasting Disease (including information on the CWD Certified and Monitored Herd Programs).

USDA APHIS Scrapie Program

United States Food and Drug Administration (FDA). Bovine Spongiform Encephalopathy

U.S. Geological Survey (USGS). Chronic Wasting Disease

World Organization for Animal Health (WOAH)

WOAH Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

WOAH Terrestrial Animal Health Code

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