Chronic Wasting Disease

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Importance

Chronic wasting disease (CWD) is a contagious neurodegenerative disease, caused by a prion, that affects cervids such as deer, elk, reindeer and moose, and is always fatal once the clinical signs appear. It is one of the most difficult diseases to control, as the incubation period is very long, cervids can shed prions before they become symptomatic, diagnostic tests do not identify some animals during the early stages, and prions may remain infectious in contaminated environments for years. Introduction of chronic wasting disease into a farmed cervid herd usually triggers a regulatory response with strict quarantine or depopulation and may result in the loss of the farmer's livelihood.

In the 1960s and 1970s, chronic wasting disease was an obscure illness mostly found only in a small geographic area in northeastern Colorado and southeastern Wyoming. However, this disease now affects wild or farmed cervids in many parts of the U.S. and Canada. Cases have been seen among captive cervids in South Korea since 2001, after infected animals were imported from Canada, and what appear to be unrelated CWD prions have been found in wild cervids in parts of Europe since 2016. Although many wild or captive cervids have been killed during attempts to control this disease in the U.S., Canada, South Korea and Norway, these efforts have mostly failed to prevent its spread in wild populations. There are also concerns that CWD prions, which cannot be destroyed by cooking, might be able to affect humans or animals other than cervids, though to date, there is no evidence that this occurs in nature.

Etiology

CWD is a member of the transmissible spongiform encephalopathies (TSEs), a group of neurodegenerative disorders caused by prions. Prions are infectious proteins that appear to replicate by converting a normal cellular protein into copies of the prion. This cellular protein, which is called PrPc, is found on the surface of neurons and various other cells in the body, but its functions are still incompletely understood. PrPc proteins differ somewhat between species of animals, and a given host's PrPc may or may not be convertible by a specific prion. Individuals within a species can also have PrPc variants that influence their susceptibility.

Pathogenic isoforms of PrPc are designated by various terms such as PrPres or PrP^{TSE} or, when referring specifically to chronic wasting disease, PrP^{CWD}. Some variants of the CWD prion, including those in North America, spread readily in cervid populations, while others seem to arise spontaneously in the CNS of individual animals, with no apparent transmission to other cervids. In Europe, the latter strains have been designated 'spontaneous (or atypical) moose CWD' and 'spontaneous (or atypical) red deer CWD,' and are analogous to spontaneously developing prions in other species, such as the genetic form of Creutzfeldt-Jakob disease (sCJD) in humans or atypical bovine spongiform encephalopathy (BSE) in cattle. Cases caused by spontaneous prions in cervids have also been designated Ly- cases, based on the absence of prions from lymphoid tissues, while contagious CWD is termed Ly+.

Species Affected

Chronic wasting disease is known to affect a number of cervid species. Naturally acquired cases have been reported in mule deer (*Odocoileus hemionus*), black-tailed deer (*O. hemionus columbianus*), white-tailed deer (*O. virginianus*), Rocky Mountain elk (*Cervus elaphus nelsoni*), red deer (*Cervus elaphus elaphus*), moose (*Alces alces*), reindeer (*Rangifer tarandus tarandus*) and sika deer (*Cervus nippon*), as well as crosses between some of these species. Reeve's muntjac deer (*Muntiacus reevesi*) have been infected by oral inoculation in the laboratory, and some other species, such as caribou (various subspecies of *R. tarandus*), are also likely to be susceptible. However, some cervids might be more resistant. Although prions replicated in fallow deer (*Cervus dama dama*) after intracerebral inoculation, prion deposition in the brain was sparse, and no fallow deer became infected after 6 or more years of exposure to infected deer and contaminated pastures.

There is currently no evidence that CWD prions have infected any animals other than cervids in nature, including domestic livestock that shared pastures with cervids

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for long periods, or carnivores and scavengers such as coyotes (*Canis latrans*), mink (*Mustela vison*), opossums (*Didelphis virginiana*) and raccoons (*Procyon lotor*) from endemic areas, though some of the latter species may transiently excrete prions in the feces after eating contaminated tissues.

Laboratory studies also seem to indicate that most animals other than cervids are not susceptible to CWD. Some researchers study hosts by direct intracerebral inoculation (injection) of prions. This method, which typically uses a high dose unlikely to reach the CNS in nature, can identify species with incompatible cellular prions that cannot propagate CWD. However, it bypasses barriers that may prevent initial infection or transport of prions to susceptible tissues, and cannot determine whether a species could be infected by a natural route such as oral exposure. Some mammals that have been identified as susceptible to intracranial inoculation of CWD include cattle, sheep, goats, pigs, ferrets, mink, cats, raccoons, squirrel monkeys (*Saimiri sciureus*) and several North American or European rodents. CWD prions do not replicate readily in most laboratory rodents, including non-transgenic mice, though hamsters are susceptible to intracerebral inoculation to a limited degree.

Some species have been investigated further by either oral dosing or controlled environmental exposure. There is particular interest in livestock, which may interact with cervids or their environments, and in felids, which seem to be particularly susceptible to certain prions such as BSE. Attempts to infect cattle, cats and other felids, ferrets and mink by feeding prions from cervids failed to infect any animals. Published studies, to date, include a 10-year experiment in 41 cattle that either dosed them once orally with a very high quantity of CWD prions or exposed them continuously to infected cervids in the same pens, as well as a long-term (18 year) feeding trial of 3 mountain lions (*Puma concolor*), which exposed them weekly to CWD-infected tissues in their diet.

A few studies have, however, suggested that some sheep, pigs or nonhuman primates might be susceptible, at least under laboratory conditions. One group reported that, in one of 7 oronasally dosed sheep, prions were found in lymphoid tissues near the inoculation site when it was killed at 5 years. This animal had no clinical signs, and prions were not detected either in the brain or in a limited selection of more distant lymphoid organs, where prions usually spread eventually in cervids. Another study reported that one orally challenged 6-year-old-pig had evidence of prions in the CNS, though not in any lymphoid tissues, using standard prion detection techniques. Using highly sensitive methods, they also found prions at low levels in the brain and/or lymphoid tissues of several other 6-month or 6-year-old pigs (though they apparently did only very limited testing of their control animals with this assay). None of the inoculated pigs had any clinical signs attributed to CWD, and no histopathological evidence of prion damage was found in the brain of any animal.

Studies in nonhuman primates, as of 2024, have reported that squirrel monkeys, which are highly susceptible to various prions, became infected after either intracranial or oral inoculation of CWD prions, while one study of cynomolgus macaques (*Macaca fascicularis*) observed for up to 13 years and an interim report from another group found no evidence of infection after intracranial, oral or intradermal inoculation. Another interim report briefly mentions not finding any evidence of infection in macaques up to 7 years after an unspecified route of exposure. A different group reported finding atypical clinical signs, subclinical infections and evidence of prion staining in some orally inoculated cynomolgus macaques at a conference in 2017, and later reported finding CWD prions in CNS tissues from experimentally infected macaques with highly sensitive techniques; however, none of their research has yet been published, and a published report of nonspecific CWD prion staining in both control and CWD-inoculated older macaques suggests caution in interpreting some of their results.

Zoonotic potential

Currently, there is no evidence for any CWD infections in humans, though the possibility cannot be ruled out. As of 2024, surveillance, investigation of potentially suspicious cases of neurological disease in humans (e.g., cases in young patients) and epidemiological studies of people who accidentally ate CWD-contaminated meat have found no evidence that this disease is zoonotic. However, the rarity of spontaneous (genetic) prion diseases in humans (1-2 cases per million persons per year) can make small changes in their epidemiology difficult to detect by surveillance.

Laboratory models have provided contradictory evidence about whether human PrPc might be converted by CWD prions. At least seven intracerebral inoculation studies in transgenic mice expressing high levels of human prion proteins found no evidence for infections, though one recent study reported that their mice were susceptible. An attempt to infect cultured human cerebral organoids with CWD prions *in vitro* was unsuccessful, while the evidence from *in vitro* prion compatibility studies is mixed.

Geographic Distribution

In 2024, chronic wasting disease was known to occur in at least 32 US states and 4 Canadian provinces, though its distribution can be patchy. South Korea found this disease in imported deer and elk in 2001, in the offspring of imported elk in 2004, and in various captive cervids from 2010 to 2016. It still appears be present on some Korean farms, based on a research article investigating CWD infections and variability in PrPc that was published in 2021.

Chronic wasting disease has also been found in wild cervids (reindeer, moose and red deer) in Norway, Sweden and Finland since 2016. European cases appear to be caused by different strains of CWD prions than those in North America, and the cases in moose and red deer, to date, appear to be spontaneous (genetic); only Norway is known to have contagious CWD in wild reindeer. It should be noted that the

prions found in moose in North America can be found in lymphoid tissues and mostly appear to be caused by the contagious North American CWD strains.

Transmission

Unlike some prion diseases, chronic wasting disease can be transmitted between cervids by direct contact. Studies have reported finding CWD prions in saliva, urine, semen, feces, antler velvet and interdigital gland secretions from at least some cervid species, with particularly high concentrations in saliva. Some secretions and excretions, including saliva, feces, urine and semen, can contain prions before the animal develops clinical signs. Most animals are thought to be infected by ingestion, including grazing in contaminated pastures; however, inhalation is also possible and there might be other routes such as sexual transmission. CWD prions have been found in the fetuses of a number of cervid species, though there has been only limited investigation of live offspring, and the disease can be transmitted experimentally between cervids by blood transfusions. These prions have also been detected in various arthropods associated with cervids, such as nasal bot larvae and ticks, but the significance of these findings, if any, is currently unclear.

CWD prions can remain infectious for long periods in the environment, and fomites are important in their transmission. Infections have been reported in cervids exposed to pastures where either infected deer had grazed 2 years earlier or an infected carcass had been left to decompose at that time. It is possible that they can persist even longer at some highly contaminated sites. Prions are known for binding to a variety of surfaces ranging from farm equipment and structures (e.g., metal, polypropylene) to plants and soil, and can retain their infectivity when bound to fomites. How long CWD prions persist in different areas seems to be influenced by the type of soil. Some soil components (e.g., montmorillonite mineral particles) bind tightly to these prions and appear to increase their longevity, while humic acid, a major component of organic matter, has been associated with decreased infectivity. Repeated cycles of wetting and drying, freeze-thaw cycles and some microorganisms (e.g., in soil, compost or lichens) also appear to degrade prions. There is at least one report that CWD prions have been found in environmental water; however, this finding needs to be confirmed, and the concentrations appeared to be very low.

Predators and scavengers that eat prions in various cervid tissues can excrete them in the feces. Coyotes have been shown to shed infectious CWD prions for up to 3 days, and crows for several hours. However, the significance of fecal shedding among carnivores is still unclear, and one study found that mountain lions fed CWD-containing meat shed only 3-4% of the prions they ingested, and no shedding occurred after the first defecation. This raises the possibility that predation might reduce CWD prion contamination in the environment rather than contributing significantly to its spread.

Disinfection

Complete decontamination of prion-contaminated tissues, surfaces and environments can be difficult. These agents are very resistant to common chemical disinfectants and can also resist heat, ultraviolet radiation, microwave emissions and ionizing radiation, particularly when they are protected in organic material or preserved with aldehyde fixatives, or when the prion titer is high. They can bind tightly to some surfaces, including stainless steel and plastic, without losing infectivity, and seem to be highly resistant to decontamination when bound to metal.

Relatively few prion decontamination techniques have been published and confirmed to be effective for routine use. Cleaning to remove organic matter, followed by either a 1-2 N sodium hydroxide solution or sodium hypochlorite with at least 2% (20,000 ppm) available chlorine, has traditionally been recommended for equipment and surfaces, with a treatment time of > 1 hour at 20°C (68°F), and overnight for some materials. Experimentally, some milder treatments (e.g., various alkaline and enzymatic detergents, a formerly marketed acidic phenolic disinfectant, hypochlorous acid, hydrogen peroxide gas plasma) were effective against certain prions, under some conditions, and might be useful for items that cannot withstand harsher chemicals. However, these agents have mainly been tested against prions other than CWD and should be validated before considering their use.

Physical inactivation of prions can be carried out by autoclaving. Guidelines on prion-specific procedures should be consulted for detailed recommendations, as resistance to heat may vary with the specific prion, degree of contamination, type of sample, and even the cleaning agent used. Prions in dried tissue films are more difficult to destroy with steam, and human guidelines recommend that surgical instruments be kept moist or wet until they are autoclaved. It may also be worth considering a combination of chemical and physical methods, which can be more effective than either alone. However, even the harshest combination of procedures is not guaranteed to destroy all prions in all types of samples.

Farm buildings and soil may be particularly difficult or impossible to decontaminate: there are reports of test sheep becoming infected with the scrapie despite the apparent absence of these prions after extensive efforts including multiple treatments with the recommended high concentrations of sodium hypochlorite. However, it should be noted that recent work suggests that sodium hydroxide (2N) may be significantly more effective than sodium hypochlorite on soil-bound prions. Incineration is commonly used for carcasses.

Incubation Period

The minimum incubation period is thought to be about 16 months, and the average incubation period is probably 2-4 years, though longer periods have been reported in animals with resistant genotypes. The maximum incubation period is not certain; however, cases have been reported in cervids that

were more than 15 years old in infected herds, where many animals are probably infected when they are young.

Clinical Signs

Chronic wasting disease begins with an asymptomatic period of varying duration, and is always fatal once the clinical signs appear. Typically, cervids develop progressive weight loss and loss of condition, accompanied by lassitude, behavioral changes and/or overt neurological signs, over several weeks to months. The CNS signs are sometimes subtle, especially early in the course of the disease or in certain species (e.g., elk), but often include ataxia, head tremors, teeth grinding, repetitive walking of an enclosure's perimeter and hyperexcitability when handled. Some affected animals carry their head low and have a fixed gaze, particularly in the late stages of disease; this can alternate with more normal alertness. Animals may have difficulty swallowing, leading to excessive salivation.

Some affected animals also develop esophageal dilation and regurgitation, and aspiration pneumonia can lead to death. Polydipsia/ polyuria and syncope may occur late in the disease, and many animals become severely emaciated before they die. Reproductive losses, including stillbirths and the deaths of offspring soon after birth, have been reported in experimentally infected muntjac deer, but many or most naturally-infected pre-symptomatic cervids seem to carry their offspring to term.

Most animals with clinical signs die within a few months, though a few may live for up to a year or more. There are, however, reports of cervids, particularly elk, that had noticeable clinical signs for only a few days before death, and stress from handling has sometimes caused sudden deaths in apparently asymptomatic animals or those with mild clinical signs.

Species other than cervids

Chronic weight loss, including severe wasting, was the most prominent sign in experimentally infected squirrel monkeys, although muscle tremors, excessive salivation and mild ataxia occurred terminally in a few animals. Intracerebrally inoculated sheep and goats developed clinical signs that resembled scrapie rather than CWD, suggesting that any cases in these animals might differ from those in cervids. No clinical signs were seen in sheep or pigs that became infected after oronasal inoculation in recent experiments.

Post Mortem Lesions

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The gross lesions are nonspecific. Some carcasses may be in good condition, with few or no lesions, particularly in the early stages of the disease; however, many are emaciated and the hair coat may be rough and dry, with patchy retention of the winter coat in summer. Megaesophagus, aspiration pneumonia and/or abomasal or omasal ulcers can be found in some individuals, while the rumen contents may be watery, frothy or contain increased amounts of sand and gravel. The urine is often dilute in animals that had access to water, but some wild cervids are dehydrated.

Diagnostic Tests

Infections in live animals are usually diagnosed by detecting prions in biopsies of lymphoid tissues, particularly rectal lymphoid tissues or palatine tonsil (other sites have also been investigated). Prions usually accumulate first in the lymphoid organs of the head and neck (e.g., the retropharyngeal lymph node) of oronasally exposed cervids, but subsequently spread to lymphoid tissues in other parts of the body and to the brain, with varying distributions and timing in different species and individuals. The standard tests to detect CWD prions are immunohistochemistry (considered to be the "gold standard"), immunoblotting (Western blotting) and rapid tests including ELISAs. Rapid tests are generally used for initial screening and confirmed by immunohistochemistry. Prions are easiest to find in animals with clinical signs, and false negatives are relatively common in the early preclinical stages.

Two highly sensitive assays, protein misfolding cyclic amplification (PMCA) and quaking-induced conversion (QuIC) or real-time quaking-induced conversion (RT-QuIC) are employed in research, and have also been considered as potential antemortem diagnostic tests. These techniques detect tiny amounts of prions by their ability to convert PrPc into CWD prions *in vitro*. However, they must be used with care and optimized for the intended use, as prolonged incubation times or high cycles in QuIC tests can result in nonspecific amplification and false positive results. Some analyses have found that, as with other diagnostic tests, false negatives may not be uncommon in the early stages of CWD when prions occur only in limited locations.

Histopathological examination of the brain can be very helpful in postmortem diagnosis. The characteristic lesions, neuronal vacuolation and non-inflammatory spongiform changes in the gray matter, are usually bilaterally symmetrical, and are most prominent in the diencephalon, olfactory cortex and nuclei of the medulla oblongata, particularly at the level of the obex. Amyloid plaques are fairly common in deer, but immunohistochemical staining is necessary to demonstrate the presence of amyloid in elk. The diagnosis can be confirmed by detecting prions in the CNS and/or the lymphoid tissues, especially the retropharyngeal lymph node. In the CNS, they are most likely to be found in the medulla oblongata at the level of the obex, and can sometimes be detected in areas that do not have spongiform changes. In autolyzed brains, CWD might be confirmed by finding characteristic prion fibrils called scrapie-associated fibrils (SAF) with electron microscopy; however, this test has low sensitivity.

Animal inoculation may be used to detect prions in special circumstances, but this technique is lengthy and labor intensive. Serology is not useful, as antibodies are not made against CWD prions.

Treatment

There is no treatment for chronic wasting disease.

Control

Disease reporting

Veterinarians who encounter or suspect chronic wasting disease should follow their national and/or local guidelines for reporting. State agencies should be consulted regarding the current regulations for farmed cervids in the U.S.

Prevention

The risk of introducing chronic wasting disease can be reduced by maintaining a closed herd or minimizing outside purchases of stock. If replacement animals must be added, they should be from herds known to be negative for this disease. Measures such as fencing (especially double perimeter fencing) can help prevent transmission from wild cervids, and other biosecurity measures, such as avoiding shared equipment, reduce the risk of acquiring prions from other farms. Regular testing may help identify infected cervids early.

Voluntary and/or mandatory programs to control or manage CWD in farmed cervids have been established in the U.S. and Canada, with eradication from captive populations as the ultimate goal. When CWD is found in captive cervids, the herd is usually quarantined. One option for the animals' disposition is a herd management plan, but most herd owners in the U.S. choose depopulation due to economic and other considerations. Initial results from one study suggest that selective breeding may reduce CWD prevalence in farmed white-tailed deer, though further research is necessary. Carcasses from CWD-infected animals cannot be used as food for other animals or people and must be destroyed.

Controlling CWD in wild cervids is very difficult. To help reduce the spread of this disease, many localities have restrictions on transporting tissues from cervids hunted in endemic areas. Some states have also banned practices that encourage cervids to congregate in certain areas (e.g., feeding or baiting) or cull wild populations to reduce their population density. Except for some predictions from artificial computer simulations (models), there is very limited and conflicting information about the effectiveness of culling strategies once CWD has become established in an area.

Morbidity and Mortality

Most cases of CWD in captive cervids occur between the ages of 2 and 7 years. An animal's genotype can influence its susceptibility to infection, the length of the incubation period and/ or the progression of clinical signs, but no cervid genotype is currently known to be completely resistant to this disease. When CWD first occurs in a herd of farmed cervids, its prevalence may be less than 1%, but in many cases, 50% or more of the herd eventually becomes infected. Despite this, only one to a few animals usually have clinical signs at any time. Chronic wasting disease is always fatal once an animal becomes symptomatic.

In wild cervids, CWD often seems to remain localized and at low prevalence for a decade or more after its introduction to a new area, which probably hinders its recognition in many cases. Excluding spontaneous CWD, free-living male cervids are more likely to be infected than females. With traditional diagnostic methods, the prevalence of CWD in North American cervids generally ranges from 1% to 30%, and is less than 5% in many affected regions. However, there are also areas with rates > 30%, especially when using highly sensitive prion detection techniques such as QuIC or PMCA. In Norway, approximately 1% of the wild reindeer were infected in the area where the initial clinical case was discovered. Although the animals in this area were all culled, a few infected reindeer continue to be found sporadically in a different wild population. The vast majority of the infections detected by surveillance programs are subclinical.

Public Health

The emergence of variant Creutzfeldt Jakob disease in people who ate meat containing the BSE prion has raised concerns about the zoonotic potential of other TSEs including chronic wasting disease. While there is currently no evidence to indicate people are susceptible to CWD, the possibility cannot be ruled out at this time. Lymphoid tissues and CNS are the most likely sources of exposure, but these prions have also been found in the meat, fat, blood and viscera of some cervids, and no tissues from infected cervids should be eaten or fed to other animals. Hunters should check with their state wildlife agencies for current precautions and information on endemic areas, and should consider having carcasses tested for CWD. The Chronic Wasting Disease Alliance website (see Internet Resources) also contains useful information for people who may come in contact with infected animals.

Veterinarians and laboratory workers should use standard precautions (e.g., the use of protective clothing and the avoidance of penetrating injuries, contamination of abraded skin, and ingestion) when conducting necropsies on CWD-suspects or handling tissues; BSL-2 is the recommended level of protection. A negative pressure laminar flow hood may be considered for some tissue manipulations. Because prions may be able to survive in the environment for years and are difficult to disinfect, contamination of surfaces and equipment should be avoided as much as possible. Some measures to consider can include the use of disposable instruments and disposable plastic-coated paper sheets to protect surfaces.

Internet Resources

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

Chronic Wasting Disease Alliance

European Food Safety Authority. Transmissible Spongiform Encephalopathies

U.S. Department of Agriculture, Animal and Plant Health Inspection Service (USDA APHIS). Chronic Wasting Disease

USDA APHIS. CWD Herd Certification Program

U.S. Geological Survey (USGS). National Wildlife Health Center

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References

Acquatella-Tran Van Ba I, Imberdis T, Perrier V. From prion diseases to prion-like propagation mechanisms of neurodegenerative diseases. Int J Cell Biol. 2013;2013:975832.

Ågren EO, Sörén K, Gavier-Widén D, Benestad SL, Tran L, Wall K, Averhed G, Doose N, Våge J, Nöremark M. First detection of chronic wasting disease in moose (*Alces alces*) in Sweden. J Wildl Dis. 2021;57(2):461-3.

Aguzzi A, Heikenwalder M, Miele G. Progress and problems in the biology, diagnostics, and therapeutics of prion diseases. J Clin Invest. 2004;114:153-60.

Anderson CA, Bosque P, Filley CM, Arciniegas DB, Kleinschmidt-Demasters BK, Pape WJ, Tyler KL. Colorado surveillance program for chronic wasting disease transmission to humans: lessons from 2 highly suspicious but negative cases. Arch Neurol. 2007;64:439-41.

Angers RC, Browning SR, Seward TS, Sigurdson CJ, Miller MW, Hoover EA, Telling GC. Prions in skeletal muscles of deer with chronic wasting disease. Science. 2006;311:1117.

Angers RC, Seward TS, Napier D, Green M, Hoover E, Spraker T, O'Rourke K, Balachandran A, Telling GC. Chronic wasting disease prions in elk antler velvet. Emerg Infect Dis. 2009;15(5):696-703.

Baeten LA, Powers BE, Jewell JE, Spraker TR, Miller MW. A natural case of chronic wasting disease in a free-ranging moose (*Alces alces shirasi*). J Wildl Dis. 2007;43:309-14.

Balachandran A, Harrington NP, Algire J, Soutyrine A, Spraker TR, Jeffrey M, González L, O'Rourke KI. Experimental oral transmission of chronic wasting disease to red deer (*Cervus elaphus elaphus*): early detection and late stage distribution of protease-resistant prion protein. Can Vet J. 2010;51(2):169-78.

Barria MA, Ironside JW, Head MW. Exploring the zoonotic potential of animal prion diseases: *in vivo* and *in vitro* approaches. Prion. 2014;8(1):85-91.

Bartz JC, Benavente R, Caughey B, Christensen S, Herbst A, Hoover EA, Mathiason CK, McKenzie D, Morales R, Schwabenlander MD, Walsh DP, The Nc North American Interdisciplinary Chronic Wasting Disease Research Consortium Members. Chronic wasting disease: state of the science. Pathogens. 2024;13(2):138.

Baune C, Wolfe LL, Schott KC, Griffin KA, Hughson AG, Miller MW, Race B. Reduction of chronic wasting disease prion seeding activity following digestion by mountain lions. mSphere. 2021;6(6):e0081221.

Belay ED, Maddox RA, Williams ES, Miller MW, Gambetti P, Schonberger LB. Chronic wasting disease and potential transmission to humans. Emerg Infect Dis. 2004;10:977-84.

Benestad SL, Telling GC. Chronic wasting disease: an evolving prion disease of cervids. Handb Clin Neurol. 2018;153:135-51.

Booth CJ, Lichtenberg SS, Chappell RJ, Pedersen JA. Chemical inactivation of prions is altered by binding to the soil mineral montmorillonite. ACS Infect Dis. 2021;7(4):859-70.

Brandt AL, Kelly AC, Green ML, Shelton P, Novakofski J, Mateus-Pinilla NE. Prion protein gene sequence and chronic wasting disease susceptibility in white-tailed deer (*Odocoileus virginianus*). Prion. 2015;9(6):449-62.

Bravo-Risi F, Soto P, Eckland T, Dittmar R, Ramírez S, Catumbela CSG, Soto C, Lockwood M, Nichols T, Morales R. Detection of CWD prions in naturally infected white-tailed deer fetuses and gestational tissues by PMCA. Sci Rep. 2021;11(1):18385.

Brown P, Abee CR. Working with transmissible spongiform encephalopathy agents. ILAR J. 2005;46:44-52.

Brown P, Rau EH, Johnson BK, Bacote AE, Gibbs CJ, Jr., Gajdusek DC. New studies on the heat resistance of hamster-adapted scrapie agent: threshold survival after ashing at 600 degrees C suggests an inorganic template of replication. Proc Natl Acad Sci USA. 2000;97:3418-21.

Cassmann ED, Moore SJ, Greenlee JJ. Experimental oronasal transmission of chronic wasting disease agent from white-tailed deer to Suffolk sheep. Emerg Infect Dis. 2021;27(12):3156-8.

Centers for Disease Control and Prevention (CDC). Chronic wasting disease [online]. CDC; 2007 Jan. Available at: http://www.cdc.gov/ncidod/dvrd/cwd/.* Accessed 19 Sept. 2008.

Chang B, Cheng X, Yin S, Pan T, Zhang H, et al. Test for detection of disease-associated prion aggregate in the blood of infected but asymptomatic animals. Clin Vaccine Immunol. 2007;14:36-43.

Chesney AR, Booth CJ, Lietz CB, Li L, Pedersen JA. Peroxymonosulfate rapidly inactivates the disease-associated prion protein. Environ Sci Technol. 2016;50(13):7095-105.

Chronic Wasting Disease Alliance. Carcass transportation regulations in the United States and Canada [online]. Available at: http://www.cwd-info.org/index.php/fuseaction/policy.main.* Accessed 19 Sept 2008.

Chronic Wasting Disease Alliance. Chronic wasting disease (CWD) outbreaks and surveillance program in the Republic of Korea. 2011. Available at: http://cwd-info.org/chronic-wasting-disease-cwd-outbreaks-and-surveillance-program-in-the-republic-of-korea/. Accessed 28 July 2016.

Chronic Wasting Disease Alliance. The first detection of chronic wasting disease (CWD) in Europe. 2016. Available at: http://cwd-info.org/the-first-detection-of-chronic-wasting-disease-cwd-in-europe/. Accessed 29 Jul 2016.

Colorado Division of Wildlife. Chronic wasting disease in Colorado, 2006–2008. Colorado Division of Wildlife Report. Fort Collins, Colorado; 2009. 5 p.

Comoy EE, Mikol J, Luccantoni-Freire S, Correia E, Lescoutra-Etchegaray N, Durand V, Dehen C, Andreoletti O, Casalone C, Richt JA, Greenlee JJ, Baron T, Benestad SL, Brown P, Deslys JP. Transmission of scrapie prions to primate after an extended silent incubation period. Sci Rep. 2015; 5:11573.

Cooper SK, Hoover CE, Henderson DM, Haley NJ, Mathiason CK, Hoover EA. Detection of CWD in cervids by RT-QuIC assay of third eyelids. PLoS One. 2019;14(8):e0221654.

Czub S, Schulz-Schaeffe W, Stahl-Hennig C, Beekes M, Schaetzl H, Motzkus D. First evidence of intracranial and peroral transmission of chronic wasting disease (CWD) into cynomolgus macaques: a work in progress. In: Prion 2017 Deciphering Neurodegenerative Disorders. Edingurgh: Taylor & Francis. 2017.

Daus ML, Breyer J, Wagenfuehr K, Wemheuer WM, Thomzig A, Schulz-Schaeffer WJ, Beekes M. Presence and seeding activity of pathological prion protein (PrP(TSE)) in skeletal muscles of white-tailed deer infected with chronic wasting disease. PLoS One. 2011;6(4):e18345.

Denkers ND, Hoover CE, Davenport KA, Henderson DM, McNulty EE, Nalls AV, Mathiason CK, Hoover EA. Very low oral exposure to prions of brain or saliva origin can transmit chronic wasting disease. PLoS One. 2020;15(8):e0237410.

EFSA Panel on Biological Hazards (BIOHAZ); Koutsoumanis K, Allende A, Alvarez-Ordoñez A, Bolton D, Bover-Cid S, et al. Monitoring of chronic wasting disease (CWD) (IV). EFSA J. 2023;21(4):e07936.

EFSA Panel on Biological Hazards (BIOHAZ); Koutsoumanis K, Allende A, Alvarez-Ordoňez A, Bolton D, Bover-Cid S, et al. Update on chronic wasting disease (CWD) III. EFSA J. 2019;17(11):e05863.

EFSA Panel on Biological Hazards (BIOHAZ); Ricci A, Allende A, Bolton D, Chemaly M, Davies R, et al. Chronic wasting disease (CWD) in cervids. EFSA J. 2017;15(1):e04667.

EFSA Panel on Biological Hazards (BIOHAZ); Ricci A, Allende A, Bolton D, Chemaly M, Davies R, et al. Scientific opinion on chronic wasting disease (II). EFSA J. 2018;16(1):e05132.

Elder AM, Henderson DM, Nalls AV, Wilham JM, Caughey BW, Hoover EA, Kincaid AE, Bartz JC, Mathiason CK. *In vitro* detection of prionemia in TSE-infected cervids and hamsters. PLoS One. 2013;8(11):e80203.

Ferreira NC, Charco JM, Plagenz J, Orru CD, Denkers ND, Metrick MA 2nd, Hughson AG, Griffin KA, Race B, Hoover EA, Castilla J, Nichols TA, Miller MW, Caughey B. Detection of chronic wasting disease in mule and white-tailed deer by RT-QuIC analysis of outer ear. Sci Rep. 2021;11(1):7702.

Fichet G, Comoy E, Dehen C, Challier L, Antloga K, Deslys JP, McDonnell G. Investigations of a prion infectivity assay to evaluate methods of decontamination. J Microbiol Methods. 2007;70:511-8.

Fichet G, Comoy E, Duval C, Antloga K, Dehen C, Charbonnier A, McDonnell G, Brown P, Lasmézas CI, Deslys JP. Novel methods for disinfection of prion-contaminated medical devices. Lancet. 2004;364:521-6.

Fischer JR, Nettles VF (College of Veterinary Medicine, The University of Georgia). National chronic wasting disease surveillance in free-ranging cervids: accomplishments and needs [online]. In: USAHA 2002 Proceedings; 2002 Oct 20-23; St. Louis, MO. Available at: http://www.usaha.org/speeches/speech02/s02cwdss.html.* Accessed 2 Dec 2003.

Gavier-Widén D, Stack MJ, Baron T, Balachandran A, Simmons M. Diagnosis of transmissible spongiform encephalopathies in animals: a review. J Vet Diagn Invest. 2005;17:509-27.

Gilch S, Chitoor N, Taguchi Y, Stuart M, Jewell JE, Schätzl HM. Chronic wasting disease. Top Curr Chem. 2011;305:51-77.

Goldmann W. PrP genetics in ruminant transmissible spongiform encephalopathies. Vet Res. 2008;39:30.

Gough KC, Baker CA, Hawkins S, Simmons H, Konold T, Maddison BC. Rapid recontamination of a farm building occurs after attempted prion removal. Vet Rec. 2019;184(3):97.

Gould DH, Voss JL, Miller MW, Bachand AM, Cummings BA, Frank AA. Survey of cattle in northeast Colorado for evidence of chronic wasting disease: geographical and high-risk targeted sample. J Vet Diagn Invest. 2003;15:274-7.

Greenlee JJ, Nicholson EM, Smith JD, Kunkle RA, Hamir AN. Susceptibility of cattle to the agent of chronic wasting disease from elk after intracranial inoculation. J Vet Diagn Invest. 2012;24(6):1087-93.

Groveman BR, Williams K, Race B, Foliaki S, Thomas T, Hughson AG, Walters RO, Zou W, Haigh CL. Lack of transmission of chronic wasting disease prions to human cerebral organoids. Emerg Infect Dis. 2024;30(6):1193-202.

Haley N, Donner R, Merrett K, Miller M, Senior K. Selective breeding for disease-resistant PRNP variants to manage chronic wasting disease in farmed whitetail deer. Genes (Basel). 2021;12(9):1396.

Haley NJ, Henderson DM, Donner R, Wyckoff S, Merrett K, Tennant J, Hoover EA, Love D, Kline E, Lehmkuhl AD, Thomsen BV. Management of chronic wasting disease in ranched elk: conclusions from a longitudinal three-year study. Prion. 2020;14(1):76-87.

Haley NJ, Henderson DM, Senior K, Miller M, Donner R. Evaluation of winter ticks (*Dermacentor albipictus*) collected from North American elk (*Cervus canadensis*) in an area of chronic wasting disease endemicity for evidence of PrP(CWD) amplification using real-time quaking-induced conversion assay. mSphere. 2021;6(4):e0051521.

Haley NJ, Hoover EA. Chronic wasting disease of cervids: current knowledge and future perspectives. Annu Rev Anim Biosci. 2015;3:305-25.

Haley NJ, Mathiason CK, Carver S, Zabel M, Telling GC, Hoover EA. Detection of chronic wasting disease prions in salivary, urinary, and intestinal tissues of deer: potential mechanisms of prion shedding and transmission. J Virol. 2011;85(13):6309-18.

Haley NJ, Mathiason CK, Zabel MD, Telling GC, Hoover EA. Detection of sub-clinical CWD infection in conventional test-negative deer long after oral exposure to urine and feces from CWD+ deer. PLoS One. 2009;4(11):e7990.

Haley NJ, Seelig DM, Zabel MD, Telling GC, Hoover EA. Detection of CWD prions in urine and saliva of deer by transgenic mouse bioassay. PLoS One. 2009;4(3):e4848.

Haley NJ, Siepker C, Walter WD, Thomsen BV, Greenlee JJ, Lehmkuhl AD, Richt JA. Antemortem detection of chronic wasting disease prions in nasal brush collections and rectal biopsy specimens from white-tailed deer by real-time quaking-induced conversion. J Clin Microbiol. 2016;54(4):1108-16.

Haley NJ, Van de Motter a, Carver S, Henderson D, Davenport K, Seelig DM, Mathiason C, Hoover E. Prion-seeding activity in cerebrospinal fluid of deer with chronic wasting disease. PLoS One. 2013;8(11):e81488.

Hamir AN, Greenlee JJ, Nicholson EM, Kunkle RA, Richt JA, Miller JM, Hall M. Experimental transmission of chronic wasting disease (CWD) from elk and white-tailed deer to fallow deer by intracerebral route: final report. Can J Vet Res. 2011;75(2):152-6.

Hamir AN, Kehrli ME Jr, Kunkle RA, Greenlee JJ, Nicholson EM, Richt JA, Miller JM, Cutlip RC. Experimental interspecies transmission studies of the transmissible spongiform encephalopathies to cattle: comparison to bovine spongiform encephalopathy in cattle. J Vet Diagn Invest. 2011;23(3):407-20.

Hamir AN, Kunkle RA, Miller JM, Cutlip RC, Richt JA, Kehrli ME Jr, Williams ES. Age-related lesions in laboratory-confined raccoons (*Procyon lotor*) inoculated with the agent of chronic wasting disease of mule deer. J Vet Diagn Invest. 2007;19(6):680-6.

Hamir AN, Kunkle RA, Nicholson EM, Miller JM, Hall SM, Schoenenbruecher H, Brunelle BW, Richt JA. Preliminary observations on the experimental transmission of chronic wasting disease (CWD) from elk and white-tailed deer to fallow deer. J Comp Pathol. 2008;138(2-3):121-30.

Hamir AN, Miller JM,Cutlip RC, Stack MJ,Chaplin MJ, Jenny AL, Williams ES. Experimental inoculation of scrapie and chronic wasting disease agents in raccoons (*Procyon lotor*). Vet Rec. 2003;153:121-3.

Hannaoui S, Cheng G, Wemheuer W, Schulz-Schaeffer WJ, Gilch S, Schatzl M. Transmission of prion infectivity from CWD-infected macaque tissues to rodent models demonstrates the zoonotic potential of chronic wasting disease (abstract). In: Prion 2022 Conference. Gottingen, Germany; Sept 13-17, 2022.

Hannaoui S, Zemlyankina I, Chang SC, Arifin MI, Béringue V, McKenzie D, Schatzl HM, Gilch S. Transmission of cervid prions to humanized mice demonstrates the zoonotic potential of CWD. Acta Neuropathol. 2022;144(4):767-84.

Happ GM, Huson HJ, Beckmen KB, Kennedy LJ. Prion protein genes in caribou from Alaska. J Wildl Dis. 2007;43:224-8.

Harpaz E, Salvesen Ø, Rauset GR, Mahmood A, Tran L, Ytrehus B, Benestad SL, Tranulis MA, Espenes A, Ersdal C. No evidence of uptake or propagation of reindeer CWD prions in environmentally exposed sheep. Acta Vet Scand. 2022;64(1):13.

Harrington RD, Baszler TV, O'Rourke KI, Schneider DA, Spraker TR, Liggitt HD, Knowles DP. A species barrier limits transmission of chronic wasting disease to mink (*Mustela vison*). J Gen Virol. 2008;89(Pt 4):1086-96.

Hawkins SA, Simmons HA, Gough KC, Maddison BC. Persistence of ovine scrapie infectivity in a farm environment following cleaning and decontamination. Vet Rec. 2015;176(4):99.

Heisey DM, Mickelsen NA, Schneider JR, Johnson CJ, Johnson CJ, Langenberg JA, Bochsler PN, Keane DP, Barr DJ. Chronic wasting disease (CWD) susceptibility of several North American rodents that are sympatric with cervid CWD epidemics. J Virol. 2010;84(1):210-5.

Henderson DM, Davenport KA, Haley NJ, Denkers ND, Mathiason CK, Hoover EA. Quantitative assessment of prion infectivity in tissues and body fluids by real-time quaking-induced conversion. J Gen Virol. 2015;96(Pt 1):210-9.

Henderson DM, Denkers ND, Hoover CE, Garbino N, Mathiason CK, Hoover EA. Longitudinal detection of prion shedding in saliva and urine by chronic wasting disease-infected deer by real-time quaking-induced conversion. J Virol. 2015;89(18):9338-47.

Henderson DM, Manca M, Haley NJ, Denkers ND, Nalls AV, Mathiason CK, Caughey B, Hoover EA. Rapid antemortem detection of CWD prions in deer saliva. PLoS One. 2013;8(9):e74377.

Holz CL, Darish JR, Straka K, Grosjean N, Bolin S, Kiupel M, Sreevatsan S. Evaluation of real-time quaking-induced conversion, ELISA, and immunohistochemistry for chronic wasting disease diagnosis. Front Vet Sci. 2022;8:824815.

Hoover CE, Davenport KA, Henderson DM, Denkers ND, Mathiason CK, Soto C, Zabel MD, Hoover EA. Pathways of prion spread during early chronic wasting disease in Deer. J Virol. 2017;91(10):e00077-17.

Hopp P, Rolandsen CM, Korpenfelt SL, Våge J, Sörén K, et al. Sporadic cases of chronic wasting disease in old moose - an epidemiological study. J Gen Virol. 2024;105.

Houston F, Andréoletti O. The zoonotic potential of animal prion diseases. Handb Clin Neurol. 2018;153:447-62.

Hughson AG, Race B, Kraus A, Sangaré LR, Robins L, Groveman BR, Saijo E, Phillips K, Contreras L, Dhaliwal V, Manca M, Zanusso G, Terry D, Williams JF, Caughey B. Inactivation of prions and amyloid seeds with hypochlorous acid. PLoS Pathog. 2016;12(9):e1005914.

Inzalaco HN, Bravo-Risi F, Morales R, Walsh DP, Storm DJ, Pedersen JA, Turner WC, Lichtenberg SS. Ticks harbor and excrete chronic wasting disease prions.Sci Rep. 2023;13(1):7838.

Jacques CN, Jenks JA, Jenny AL, Griffin SL. Prevalence of chronic wasting disease and bovine tuberculosis in free-ranging deer and elk in South Dakota. J Wildl Dis. 2003;39:29-34.

Jennelle CS, Samuel MD, Nolden CA, Keane DP, Barr DJ, Johnson C, Vanderloo JP, Aiken JM, Hamir AN, Hoover EA. Surveillance for transmissible spongiform encephalopathy in scavengers of white-tailed deer carcasses in the chronic wasting disease area of Wisconsin. J Toxicol Environ Health A. 2009;72(17-18):1018-24.

Jewell JE, Brown J, Kreeger T, Williams ES. Prion protein in cardiac muscle of elk (*Cervus elaphus* nelsoni) and white-tailed deer (*Odocoileus virginianus*) infected with chronic wasting disease. J Gen Virol. 2006;87:3443-50.

Johnson CJ, Bennett JP, Biro SM, Duque-Velasquez JC, Rodriguez CM, Bessen RA, Rocke TE. Degradation of the disease-associated prion protein by a serine protease from lichens. PLoS One. 2011;6:e19836.

Keane D, Barr D, Osborn R, Langenberg J, O'Rourke K, Schneider D, Bochsler P.Validation of use of rectoanal mucosa-associated lymphoid tissue for immunohistochemical diagnosis of chronic wasting disease in white-tailed deer (*Odocoileus virginianus*). J Clin Microbiol. 2009;47(5):1412-7.

Kim TY, Shon HJ, Joo YS, Mun UK, Kang KS, Lee YS. Additional cases of chronic wasting disease in imported deer in Korea. J Vet Med Sci. 2005;67:753-9.

Kong Q, Huang S, Zou W, Vanegas D, Wang M, et al. Chronic wasting disease of elk: transmissibility to humans examined by transgenic mouse models. J Neurosci. 2005;25:7944-9.

Kraft CN, Denkers ND, Mathiason CK, Hoover EA. Longitudinal detection of prion shedding in nasal secretions of CWD-infected white-tailed deer. J Gen Virol. 2023;104(1):001825.

Kramm C, Gomez-Gutierrez R, Soto C, Telling G, Nichols T, Morales R. *In vitro* detection of chronic wasting disease (CWD) prions in semen and reproductive tissues of white tailed deer bucks (*Odocoileus virginianus*). PLoS One. 2019;14(12):e0226560.

Kramm C, Pritzkow S, Lyon A, Nichols T, Morales R, Soto C. Detection of prions in blood of cervids at the asymptomatic stage of chronic wasting disease.Sci Rep. 2017;7(1):17241.

Kramm C, Soto P, Nichols TA, Morales R. Chronic wasting disease (CWD) prion detection in blood from pre-symptomatic white-tailed deer harboring PRNP polymorphic variants. Sci Rep. 2020;10(1):19763.

Kreeger T. Distribution and status of chronic wasting disease in Wyoming [abstract]. In: National chronic wasting disease symposium [online]. 2002 Aug 6-7; Denver, CO. Available at: http://www.cwd-info.org/index.php/fuseaction/resources.symposiumAbstracts/#23.* Accessed 22 Nov 2003.

Kreeger TJ, Montgomery DL, Jewell JE, Schultz W, Williams ES. Oral transmission of chronic wasting disease in captive Shira's moose. J Wildl Dis. 2006;42:640-5.

Kurt TD, Sigurdson CJ. Cross-species transmission of CWD prions. Prion. 2016;10(1):83-91.

Kuznetsova A, Cullingham C, McKenzie D, Aiken JM. Soil humic acids degrade CWD prions and reduce infectivity. PLoS Pathog. 2018;14(11):e1007414.

Kuznetsova A, McKenzie D, Cullingham C, Aiken JM. Long-term incubation PrP(CWD) with soils affects prion recovery but not infectivity. Pathogens. 2020;9(4):311.

Kuznetsova A, McKenzie D, Ytrehus B, Utaaker KS, Aiken JM. Movement of chronic wasting disease prions in prairie, boreal and alpine soils. Pathogens. 2023;12(2):269.

Lee YH, Sohn HJ, Kim MJ, Kim HJ, Park KJ, Lee WY, Yun EI, Tark DS, Choi YP, Cho IS, Balachandran A. Experimental chronic wasting disease in wild type VM mice. J Vet Med Sci. 2013;75(8):1107-10.

Maddison BC, Owen JP, Bishop K, Shaw G, Rees HC, Gough KC. The interaction of ruminant PrP(Sc) with soils is influenced by prion source and soil type. Environ Sci Technol. 2010;44(22):8503-8.

Manjerovic MB, Green ML, Mateus-Pinilla N, Novakofski J. The importance of localized culling in stabilizing chronic wasting disease prevalence in white-tailed deer populations. Prev Vet Med. 2014;113(1):139-45.

Marín-Moreno A, Benestad SL, Barrio T, Pirisinu L, Espinosa JC, et al. Classical BSE dismissed as the cause of CWD in Norwegian red deer despite strain similarities between both prion agents. Vet Res. 2024;55(1):62.

Marsh RF, Kincaid AE, Bessen RA, Bartz JC. Interspecies transmission of chronic wasting disease prions to squirrel monkeys (*Saimiri sciureus*). J Virol. 2005;79:13794-6.

Martin S, Jeffrey M, González L, Sisó S, Reid HW, Steele P, Dagleish MP, Stack MJ, Chaplin MJ, Balachandran A. Immunohistochemical and biochemical characteristics of BSE and CWD in experimentally infected European red deer (*Cervus elaphus elaphus*). BMC Vet Res. 2009;5:26.

Mathiason CK. Large animal models for chronic wasting disease. Cell Tissue Res. 2023;392(1):21-31.

Mathiason CK, Hays SA, Powers J, Hayes-Klug J, Langenberg J, Dahmes SJ, Osborn DA, Miller KV, Warren RJ, Mason GL, Hoover EA. Infectious prions in pre-clinical deer and transmission of chronic wasting disease solely by environmental exposure. PLoS One. 2009;4(6):e5916.

Mathiason CK, Powers JG, Dahmes SJ, Osborn DA, Miller KV, et al. Infectious prions in the saliva and blood of deer with chronic wasting disease. Science. 2006;314:133-6.

Matsuura Y, Ishikawa Y, Bo X, Murayama Y, Yokoyama T, Somerville RA, Kitamoto T, Mohri S. Quantitative analysis of wet-heat inactivation in bovine spongiform encephalopathy. Biochem Biophys Res Commun. 2013;432(1):86-91.

Mazza M, Tran L, Loprevite D, Cavarretta MC, Meloni D, Dell'Atti L, Våge J, Madslien K, Vuong TT, Bozzetta E, Benestad SL. Are rapid tests and confirmatory western blot used for cattle and small ruminants TSEs reliable tools for the diagnosis of chronic wasting disease in Europe? PLoS One. 2023;18(8):e0286266.

McDonnell G, Dehen C, Perrin A, Thomas V, Igel-Egalon A, Burke PA, Deslys JP, Comoy E. Cleaning, disinfection and sterilization of surface prion contamination. J Hosp Infect. 2013;85(4):268-73.

Miller MW, Wild MA. Epidemiology of chronic wasting disease in captive white-tailed and mule deer. J Wildl Dis. 2004;40:320-7.

Miller MW, Williams ES, Hobbs NT, Wolfe LL. Environmental sources of prion transmission in mule deer. Emerg Infect Dis. 2004;10:1003-6.

Mitchell GB, Sigurdson CJ, O'Rourke KI, Algire J, Harrington NP, Walther I, Spraker TR, Balachandran A. Experimental oral transmission of chronic wasting disease to reindeer (*Rangifer tarandus tarandus*). PLoS One. 2012;7(6):e39055.

Monello RJ, Powers JG, Hobbs NT, Spraker TR, O'Rourke KI, Wild MA. Efficacy of antemortem rectal biopsies to diagnose and estimate prevalence of chronic wasting disease in free-ranging cow elk (*Cervus elaphus nelsoni*). Wildl Dis. 2013;49(2):270-8.

Moore SJ, West Greenlee MH, Kondru N, Manne S, Smith JD, Kunkle RA, Kanthasamy A, Greenlee JJ. Experimental transmission of the chronic wasting disease agent to swine after oral or intracranial inoculation. J. Virol. 2017;91(19):e00926-17.

Moore SJ, Smith JD, Richt JA, Greenlee JJ. Raccoons accumulate PrPSc after intracranial inoculation of the agents of chronic wasting disease or transmissible mink encephalopathy but not atypical scrapie. J Vet Diagn Investig. 2019;31:1040638718825290.

Mori J, Rivera N, Novakofski J, Mateus-Pinilla N. A review of chronic wasting disease (CWD) spread, surveillance, and control in the United States captive cervid industry. Prion. 2024;18(1):54-67.

Nafe R, Arendt CT, Hattingen E. Human prion diseases and the prion protein - what is the current state of knowledge? Transl Neurosci. 2023;14(1):20220315.

Nalls AV, McNulty E, Hoover CE, Pulscher LA, Hoover EA, Mathiason CK. Infectious prions in the pregnancy microenvironment of chronic wasting disease-infected Reeves' muntjac deer. J Virol. 2017;91(15):e00501-17.

Nalls AV, McNulty EE, Mayfield A, Crum JM, Keel MK, Hoover EA, Ruder MG, Mathiason CK. Detection of chronic wasting disease prions in fetal tissues of free-ranging white-tailed deer. Viruses. 2021;13(12):2430.

Nalls AV, McNulty E, Powers J, Seelig DM, Hoover C, Haley NJ, Hayes-Klug J, Anderson K, Stewart P, Goldmann W, Hoover EA, Mathiason CK. Mother to offspring transmission of chronic wasting disease in Reeves' muntjac deer. PLoS One. 2013;8(8):e71844.

Ness A, Zeng D, Kuznetsova A, Otero A, Kim C, Saboraki K, Lingle S, Pybus M, Aiken J, Gilch S, McKenzie D. Chronic wasting disease prions in mule deer interdigital glands. PLoS One. 2022;17(10):e0275375.

Nichols TA, Fischer JW, Spraker TR, Kong Q, VerCauteren KC. CWD prions remain infectious after passage through the digestive system of coyotes (*Canis latrans*). Prion. 2015;9(5):367-75.

Nichols TA, Pulford B, Wyckoff AC, Meyerett C, Michel B, Gertig K, Hoover EA, Jewell JE, Telling GC, Zabel MD. Detection of protease-resistant cervid prion protein in water from a CWD-endemic area. Prion. 2009;3(3):171-83.

Nichols TA, Spraker TR, Gidlewski T, Powers JG, Telling GC, VerCauteren KC, Zabel MD. Detection of prion protein in the cerebrospinal fluid of elk (*Cervus canadensis nelsoni*) with chronic wasting disease using protein misfolding cyclic amplification. J Vet Diagn Invest. 2012;24(4):746-9.

Nichols TA, Spraker TR, Rigg TD, Meyerett-Reid C, Hoover C, Michel B, Bian J, Hoover E, Gidlewski T, Balachandran A, O'Rourke K, Telling GC, Bowen R, Zabel MD, VerCauteren KC. Intranasal inoculation of white-tailed deer (*Odocoileus virginianus*) with lyophilized chronic wasting disease prion particulate complexed to montmorillonite clay. PLoS One. 2013;8(5):e62455.

Norwegian Food Safety Authority. Chronic wasting disease in Norway. 2016. Available at: http://www.mattilsynet.no/language/english/animals/chronic_wasting_disease_in_norway.23274.* Accessed 28 Jul 2016.

Olszowy KM, Lavelle J, Rachfal K, Hempstead S, Drouin K, Darcy JM 2nd, Reiber C, Garruto RM. Six-year follow-up of a point-source exposure to CWD contaminated venison in an Upstate New York community: risk behaviours and health outcomes 2005-2011. Public Health. 2014;128(9):860-8.

Picasso-Risso C, Schwabenlander MD, Rowden G, Carstensen M, Bartz JC, Larsen PA, Wolf TM. Assessment of real-time quaking-induced conversion (RT-QuIC) assay, immunohistochemistry and ELISA for detection of chronic wasting disease under field conditions in white-tailed deer: a Bayesian approach. Pathogens. 2022;11(5):489.

Plummer IH, Wright SD, Johnson CJ, Pedersen JA, Samuel MD. Temporal patterns of chronic wasting disease prion excretion in three cervid species. J Gen Virol. 2017;98(7):1932-42.

Pritzkow S, Gorski D, Ramirez F, Telling GC, Benestad SL, Soto C. North American and Norwegian chronic wasting disease prions exhibit different potential for interspecies transmission and zoonotic risk. J Infect Dis. 2022;225(3):542-51.

Pritzkow S, Morales R, Moda F, Khan U, Telling GC, Hoover E, Soto C. Grass plants bind, retain, uptake, and transport infectious prions. Cell Rep. 2015;11(8):1168-75.

Pulford B, Spraker TR, Wyckoff AC, Meyerett C, Bender H, Ferguson A, Wyatt B, Lockwood K, Powers J, Telling GC, Wild MA, Zabel MD. Detection of PrPCWD in feces from naturally exposed Rocky Mountain elk (*Cervus elaphus nelsoni*) using protein misfolding cyclic amplification. J Wildl Dis. 2012;48(2):425-34.

Race B, Meade-White KD, Miller MW, Barbian KD, Rubenstein R, et al. Susceptibilities of nonhuman primates to chronic wasting disease. Emerg Infect Dis. 2009;15(9):1366-76.

Race B, Meade-White KD, Phillips K, Striebel J, Race R, Chesebro B. Chronic wasting disease agents in nonhuman primates. Emerg Infect Dis. 2014;20(5):833-7.

Race B, Meade-White K, Race R, Chesebro B. Prion infectivity in fat of deer with chronic wasting disease. J Virol. 2009;83(18):9608-10.

Race BL, Meade-White KD, Ward A, Jewell J, Miller MW, Williams ES, Chesebro B, Race RE. Levels of abnormal prion protein in deer and elk with chronic wasting disease. Emerg Infect Dis. 2007;13:824-30.

Race B, Williams K, Orrú CD, Hughson AG, Lubke L, Chesebro B. Lack of transmission of chronic wasting disease to cynomolgus macaques. J Virol. 2018;92(14):e00550-18.

Raymond GJ, Raymond LD, Meade-White KD, Hughson AG, Favara C, Gardner D, Williams ES, Miller MW, Race RE, Caughey B. Transmission and adaptation of chronic wasting disease to hamsters and transgenic mice: evidence for strains. J Virol. 2007;81:4305-14.

Rhyan JC, Miller MW, Spraker TR, McCollum M, Nol P, Wolfe LL, Davis TR, Creekmore L, O'Rourke KI. Failure of fallow deer (*Dama dama*) to develop chronic wasting disease when exposed to a contaminated environment and infected mule deer (*Odocoileus hemionus*). J Wildl Dis. 2011;47(3):739-44.

Roh I-S, KimY-C, Kim H-J,Won S-Y, JeongM-J, Hwang J-Y, Kang H-E, Sohn H-J, Jeong B-H. Polymorphisms of the prion-related protein gene are strongly associated with cervids' susceptibility to chronic wasting disease. Vet Rec. 2021;e940.

Robinson SJ, Samuel MD, O'Rourke KI, Johnson CJ. The role of genetics in chronic wasting disease of North American cervids. Prion. 2012;6(2):153-62.

Rogez-Kreuz C, Yousfi R, Soufflet C, Quadrio I, Yan ZX, Huyot V, Aubenque C, Destrez P, Roth K, Roberts C, Favero M, Clayette P. Inactivation of animal and human prions by hydrogen peroxide gas plasma sterilization. Infect Control Hosp Epidemiol. 2009;30(8):769-77.

Rubenstein R, Chang B, Gray P, Piltch M, Bulgin MS, Sorensen-Melson S, Miller MW. Prion disease detection, PMCA kinetics, and IgG in urine from sheep naturally/experimentally infected with scrapie and deer with preclinical/clinical chronic wasting disease. J Virol. 2011;85(17):9031-8.

Rutala WA, Weber DJ; Society for Healthcare Epidemiology of America. Guideline for disinfection and sterilization of prion-contaminated medical instruments. Infect Control Hosp Epidemiol. 2010;31(2):107-17.

Saunders SE, Bartelt-Hunt SL, Bartz JC. Occurrence, transmission, and zoonotic potential of chronic wasting disease. Emerg Infect Dis. 2012;18(3):369-76.

Saunders SE, Bartz JC, Telling GC, Bartelt-Hunt SL. Environmentally-relevant forms of the prion protein. Environ Sci Technol. 2008;42(17):6573-9.

Saunders SE, Bartz JC, Vercauteren KC, Bartelt-Hunt SL. An enzymatic treatment of soil-bound prions effectively inhibits replication. Appl Environ Microbiol. 2011;77(13):4313-7.

Schneider DA, Lehmkuhl AD, Spraker TR, Dittmar RO, Lockwood MA, Rollo S, Nichols TA. Tonsil biopsy to detect chronic wasting disease in white-tailed deer (*Odocoileus virginianus*) by immunohistochemistry. PLoS One. 2023;18(3):e0282356.

Schuler KL, Jenks JA, DePerno CS, Wild MA, Swanson CC. Tonsillar biopsy test for chronic wasting disease: Two sampling approaches in mule deer and white-tailed deer. J Wildl Dis. 2005;41:820-4.

Schwabenlander MD, Culhane MR, Hall SM, Goyal SM, Anderson PL, Carstensen M, Wells SJ, Slade WB, Armién AG. A case of chronic wasting disease in a captive red deer (*Cervus elaphus*). J Vet Diagn Invest. 2013;25(5):573-6.

Seelig DM, Nalls AV, Flasik M, Frank V, Eaton S, Mathiason CK, Hoover EA. Lesion profiling and subcellular prion localization of cervid chronic wasting disease in domestic cats. Vet Pathol. 2015;52(1):107-19.

Seidel B, Thomzig A, Buschmann A, Groschup MH, Peters R, Beekes M, Terytze K. Scrapie agent (strain 263K) can transmit disease via the oral route after persistence in soil over years. PLoS ONE. 2007;2(5):e435.

Selariu A, Powers JG, Nalls A, Brandhuber M, Mayfield A, Fullaway S, Wyckoff CA, Goldmann W, Zabel MM, Wild MA, Hoover EA, Mathiason CK. *In utero* transmission and tissue distribution of chronic wasting disease-associated prions in free-ranging Rocky Mountain elk. J Gen Virol. 2015;96(11):3444-55.

Shikiya RA, Kincaid AE, Bartz JC, Bourret TJ. Failure to detect prion infectivity in ticks following prion-infected blood meal. mSphere. 2020;5(5):e00741-20.

Sigurdson CJ, Aguzzi A. Chronic wasting disease. Biochim Biophys Acta. 2007;1772:610-8.

Sigurdson CJ, Mathiason CK, Perrott MR, Eliason GA, Spraker TR, Glatzel M, Manco G, Bartz JC, Miller MW, Hoover EA. Experimental chronic wasting disease (CWD) in the ferret. J Comp Pathol. 2008;138(4):189-96.

Smith CB, Booth CJ, Pedersen JA. Fate of prions in soil: a review. J Environ Qual. 2011;40(2):449-61.

Smith JD, Nicholson EM, Greenlee JJ. Evaluation of a combinatorial approach to prion inactivation using an oxidizing agent, SDS, and proteinase K. BMC Vet Res. 2013;9:151.

Sohn HJ, Kim JH, Choi KS, Nah JJ, Joo YS, Jean YH, Ahn SW, Kim OK, Kim DY, Balachandran A. A case of chronic wasting disease in an elk imported to Korea from Canada. J Vet Med Sci. 2002;64:855-8.

Sohn HJ, Mitchell G, Lee YH, Kim HJ, Park KJ, Staskevicus A, Walther I, Soutyrine A, Balachandran A. Experimental oral transmission of chronic wasting disease to sika deer (*Cervus nippon*). Prion. 2020;14(1):271-7.

Sohn HJ, Park KJ, Roh IS, Kim HJ, Park HC, Kang HE. Sodium hydroxide treatment effectively inhibits PrP(CWD) replication in farm soil. Prion. 2019;13(1):137-40.

Sola D, Tran L, Våge J, Madslien K, Vuong TT, Korpenfelt SL, Ågren EO, Averhed G, Nöremark M, Sörén K, Isaksson M, Acín C, Badiola JJ, Gavier-Widén D, Benestad SL. Heterogeneity of pathological prion protein accumulation in the brain of moose (*Alces alces*) from Norway, Sweden and Finland with chronic wasting disease.Vet Res. 2023;54(1):74.

Somerville RA, Gentles N. Characterization of the effect of heat on agent strains of the transmissible spongiform encephalopathies. J Gen Virol. 2011;92(Pt 7):1738-48.

Soto P, Bravo-Risi F, Kramm C, Gamez N, Benavente R, Bonilla DL, Reed JH, Lockwood M, Spraker TR, Nichols T, Morales R. Nasal bots carry relevant titers of CWD prions in naturally infected white-tailed deer. EMBO Rep. 2024;25(1):334-50.

Spraker TR, Gidlewski TL, Balachandran A, VerCauteren KC, Creekmore L, Munger RD. Detection of PrP(CWD) in postmortem rectal lymphoid tissues in Rocky Mountain elk (*Cervus elaphus* nelsoni) infected with chronic wasting disease. J Vet Diagn Invest. 2006;18:553-7.

Spraker TR, Gidlewski T, Powers JG, Nichols TA, Wild MA. Distribution of the misfolded isoform of the prion protein in peripheral tissues and spinal cord of Rocky Mountain elk (*Cervus elaphus nelsoni*) with naturally occurring chronic wasting disease. Vet Pathol. 2023;60(4):420-33.

Spraker TR, VerCauteren KC, Gidlewski T, Schneider DA, Munger R, Balachandran A, O'Rourke KI. Antemortem detection of PrPCWD in preclinical, ranch-raised Rocky Mountain elk (*Cervus elaphus* nelsoni) by biopsy of the rectal mucosa. J Vet Diagn Invest. 2009;21(1):15-24.

Tamgüney G, Miller MW, Wolfe LL, Sirochman TM, Glidden DV, Palmer C, Lemus A, DeArmond SJ, Prusiner SB. Asymptomatic deer excrete infectious prions in faeces. Nature. 2009;461(7263):529-32.

Thomsen BV, Schneider DA, O'Rourke KI, Gidlewski T, McLane J, Allen RW, McIsaac AA, Mitchell GB, Keane DP, Spraker TR, Balachandran A. Diagnostic accuracy of rectal mucosa biopsy testing for chronic wasting disease within white-tailed deer (*Odocoileus virginianus*) herds in North America: effects of age, sex, polymorphism at PRNP codon 96, and disease progression. J Vet Diagn Invest. 2012;24(5):878-87.

Tranulis MA, Tryland M. The zoonotic potential of chronic wasting disease- a review. Foods. 2023;12(4):824.

Uehlinger FD, Johnston AC, Bollinger TK, Waldner CL. Systematic review of management strategies to control chronic wasting disease in wild deer populations in North America. BMC Vet Res. 2016;12(1):173.

U.S. Department of Agriculture, Animal and Plant Health Inspection Service [USDA APHIS]. Transmissible spongiform encephalopathies [online]. USDA APHIS; 2000 July. Available at: http://www.aphis.usda.gov/oa/pubs/fstse.html.* Accessed 7 Nov 2001.

VerCauteren KC, Pilon JL, Nash PB, Phillips GE, Fischer JW. Prion remains infectious after passage through digestive system of American crows (*Corvus brachyrhynchos*). PLoS One. 2012;7(10):e45774.

Vikøren T, Våge J, Madslien KI, Røed KH, Rolandsen CM, et al. First detection of chronic wasting disease in a wild red deer (*Cervus elaphus*) in Europe. J Wildl Dis. 2019;55(4):970-2.

Waddell L, Greig J, Mascarenhas M, Otten A, Corrin T, Hierlihy K. Current evidence on the transmissibility of chronic wasting disease prions to humans-A systematic review. Transbound Emerg Dis. 2018;65(1):37-49.

Wadsworth JDF, Joiner S, Linehan JM, Jack K, Al-Doujaily H, et al. Humanized transgenic mice are resistant to chronic wasting disease prions from Norwegian reindeer and moose. J Infect Dis. 2022;226(5):933-7.

Williams ES. Chronic wasting disease. Vet Pathol. 2005;42:530-49.

Williams ES, O'Toole D, Miller MW, Kreeger TJ, Jewell JE. Cattle (*Bos taurus*) resist chronic wasting disease following oral inoculation challenge of ten years' natural exposure in contaminated environments. J Wildl Dis. 2018;54(3):460-70.

Williams K, Hughson AG, Chesebro B, Race B. Inactivation of chronic wasting disease prions using sodium hypochlorite. PLoS One. 2019;14(10):e0223659.

Wolfe LL, Fox KA, Miller MW. "Atypical" chronic wasting disease in PRNP genotype 225FF mule deer. J Wildl Dis. 2014;50(3):660-5.

Wolfe LL, Fox KA, Griffin KA, Miller MW. Mountain lions (*Puma concolor*) resist long-term dietary exposure to chronic wasting disease. J Wildl Dis. 2022;58(1):40-9.

Wolfe LL, Watry MK, Sirochman MA, Sirochman TM, Miller MW. Evaluation of a test and cull strategy for reducing prevalence of chronic wasting disease in mule deer (*Odocoileus hemionus*). J Wildl Dis. 2018;54(3):511-19.

Xu S, Reuter T, Gilroyed BH, Mitchell GB, Price LM, Dudas S, Braithwaite SL, Graham C, Czub S, Leonard JJ, Balachandran A, Neumann NF, Belosevic M, McAllister TA. Biodegradation of prions in compost. Environ Sci Technol. 2014;48(12):6909-18.

Yilmaz G, Morrill T, Pilot W, Ward C, Mitchell G, Soutyrine A, Dan H, Lin M, Guan J. Optimization of RT-QuIC assay duration for screening chronic wasting disease in white-tailed deer. Vet Sci. 2024;11(2):60.

Yuan Q, Eckland T, Telling G, Bartz J, Bartelt-Hunt S. Mitigation of prion infectivity and conversion capacity by a simulated natural process--repeated cycles of drying and wetting. PLoS Pathog. 2015;11(2):e1004638.

Yuan Q, Telling G, Bartelt-Hunt SL, Bartz JC. Dehydration of prions on environmentally relevant surfaces protects them from inactivation by freezing and thawing. J Virol. 2018;92(8):e02191-17.

*Link is defunct

