Chronic Wasting Disease

Importance

Chronic wasting disease (CWD) is a neurodegenerative disease, caused by a prion that affects cervids including deer, elk and moose. Until recently, CWD was an obscure illness that seemed to be found only in a small geographic area in northeastern Colorado and southeastern Wyoming. However, this disease has now been detected in wild and farmed cervids in many other U.S. states and Canada. Korea reported outbreaks in captive cervids imported from Canada, as well as in their offspring. Chronic wasting disease can be devastating in farmed herds. This disease is always fatal once the symptoms appear, and most or all of the herd can eventually become infected. It is one of the most difficult prion diseases to control: CWD prions are transmitted from animal to animal, as well as from contaminated environments for two years or more. This disease is also endemic in wild populations. More than 12,000 captive elk and thousands of wild deer and elk have been killed in the U.S. and Canada in control efforts. In addition, there are concerns about the possible impact of CWD on humans. Cooking does not destroy prions, and ingestion of another prion, the agent that causes bovine spongiform encephalopathy (BSE), has been linked to a fatal human neurologic disease. CWD prions have been found in muscle (meat), as well as other tissues of cervids, and could enter the food supply. Although the evidence so far suggests that CWD probably does not affect humans, the possibility that it could be zoonotic has not been ruled out.

Etiology

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

Species Affected

Chronic wasting disease affects cervids including mule deer (Odocoileus hemionus), black-tailed deer (O. hemionus columbianus), white-tailed deer (O. virginianus) and Rocky Mountain elk (Cervus elaphus nelsoni). Recently, infections have been described in both wild and experimentally infected moose (Alces alces). Other cervids such as red deer (Cervus elaphus elaphus) and reindeer/caribou (Rangifer tarandus) may also be susceptible; the normal PrPc proteins found in these animals are very similar to the proteins found in affected species.

There is currently no evidence that CWD prions infect domesticated animals other than captive cervids. Many non-cervid species including cattle, sheep, goats, ferrets, mink, raccoons and squirrel monkeys have been infected, but only by direct intracerebral inoculation. Attempts to infect cattle by feeding prions have failed. Epidemiological studies also suggest that cattle are unlikely to be susceptible: chronic wasting disease has not been reported in any cattle co-pastured with deer or elk, or in surveys of cattle in endemic areas. Oral challenge studies have not been published for sheep and goats, but some molecular studies suggest that the species barriers to CWD prion replication may be lower in sheep than cattle. Oral inoculation was unable to infect ferrets or mink. CWD prions do not replicate readily in most laboratory rodents, although hamsters are susceptible to intracerebral inoculation to a limited degree. Wild-type mice are not susceptible, but transgenic mice expressing cervid proteins are being developed.

CWD prions have not been reported in humans, but the possibility that this disease could be zoonotic has not been ruled out.
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Geographic Distribution

Chronic wasting disease is endemic in the United States and Canada. This disease was originally reported only from a limited area encompassing northeastern Colorado, southwestern Nebraska, and southeastern Wyoming; however, recent surveillance suggests it is currently more widespread. CWD has been identified in at least 14 U.S. states and two Canadian provinces. As of 2008, this disease has been found in wild deer and elk populations extending from the original focus in Colorado and Wyoming east to New York and West Virginia, as well as in distinct foci in Utah and New Mexico. This infection has also been reported in captive cervid herds in a number of U.S. states. In some wild populations, CWD occurs in focal areas separated by long distances, and may be associated with transmission from captive herds, imported animals or game farms. In others, it seems to have been spread by the natural movement of wild cervids.

Chronic wasting disease was reported in imported deer and elk in Korea in 2001 and in the offspring of imported elk in 2004; no infections were reported in indigenous cervids. Limited surveillance in Europe has not revealed any evidence of this disease to date. Whether CWD has been imported to other countries is unknown.

Transmission

Chronic wasting disease seems to spread horizontally between animals by direct contact, environmental contamination or a combination of these routes. Transmission is linked to the presence of CWD prions in lymphoid tissues such as the tonsils. Elk, which have relatively small amounts of prions in these tissues, transmit CWD less efficiently than deer. Moose also have prions in lymphoid tissues, although horizontal transmission has not yet been proven in this species. In deer, CWD prions are known to occur in saliva and blood; they can be transmitted experimentally between animals by oral inoculation of saliva, as well as by blood transfusion. How quickly animals become infectious is unknown; in one study, prions were found in the tonsils between 3 and 12 months after inoculation. Whether CWD prions can be shed in milk, urine or feces is unknown. Prions have also been detected in the skeletal muscles of deer, and in heart muscle from white-tailed deer and elk. The occurrence of prions in blood suggests that no tissues from infected cervids should be considered prion-free. Vertical transmission may be possible, but it has not been documented, and does not seem to be a major route of spread.

CWD prions seem to persist for a few years in the environment. Cases have been reported after exposure to infected carcasses left to decompose in pastures approximately two years earlier. Infectivity was also reported on pastures more than two years after deer with CWD were removed.

Incubation Period

The minimum incubation period is approximately 16 months, and the average incubation period is probably 2 to 4 years. The peak incidence occurs between the ages of two and seven years. Much longer incubation periods may also be possible; in herds where CWD is endemic, cases have been reported in animals that were more than 15 years old.

Clinical Signs

Chronic wasting disease is always fatal. Some deer with subclinical or early clinical disease may die suddenly after handling. However, typically deer and elk develop progressive weight loss, lassitude and behavioral changes over several weeks to months, with many animals becoming severely emaciated before they die. Ataxia, head tremors, teeth grinding, repetitive walking of the enclosure’s perimeter, hyperexcitability when handled, or other neurologic signs may be seen; however, neurologic signs and behavioral changes are sometimes subtle, particularly in elk. In some animals, difficulty swallowing may lead to excessive salivation. Esophageal dilation and regurgitation, as well as aspiration pneumonia, have also been reported. Affected animals may carry their head low and have a fixed gaze, particularly in the late stages of disease; this can alternate with more normal alertness. Other signs that may be seen late include polydipsia/polyuria and syncope. Pruritus has not been reported in cervids; however, the coat may be rough and dry, with patchy retention of the winter coat in summer. Most affected animals die within a few months, although a few may live for up to a year or more. Occasionally, the disease may last only a few days, particularly in elk. Whether moose develop clinical signs is unknown.

Clinical signs have been reported in other species only after experimental inoculation by the intracerebral route. Sheep and goats developed symptoms that resembled scrapie, and squirrel monkeys had progressive neurological disease.

Post Mortem Lesions

The gross lesions are nonspecific. The carcass is often emaciated in the later stages of disease, and the hair coat may be rough and dry, with patchy retention of the winter coat in summer. Megasophasagus and aspiration bronchopneumonia are seen in some ruminants. The rumen contents are often watery, and may be frothy or contain increased amounts of sand and gravel. Abomasal or omasal ulcers may be found. The urine is often dilute in animals that had access to water, but some wild cervids are dehydrated. Some carcasses may be in good condition, particularly in the early stages of the disease.

The characteristic histopathologic lesions are confined to the central nervous system (CNS). In CWD, microscopic changes are most prominent in the diencephalon, olfactory cortex and nuclei of the medulla oblongata (particularly at the level of the obex), but milder changes can be found in...
other areas of the brain and spinal cord. Neuronal vacuolation and non-inflammatory spongiform changes in the gray matter are pathognomonic. Amyloid plaques may be seen. Amyloid plaques are fairly common in deer, but immuno-histochemical staining is necessary to demonstrate the presence of amyloid in elk. Lesions are usually bilaterally symmetrical.

**Morbidity and Mortality**

Chronic wasting disease is always fatal once the symptoms appear. Most cases in captive cervids occur between the ages of two and seven years. The genotype may have some influence on susceptibility and/or the length of the incubation period, but no cervid genotype appears to be completely resistant to CWD.

The incidence varies with the geographic region and species. It also differs between wild populations and captive herds. In newly infected herds of farmed cervids, the prevalence may be less than 1%. However, once the disease has become established, 50% of the herd or more often becomes infected, and in some cases, the incidence may be as high as 100%. Generally, only one animal shows signs of disease at a time. CWD is less common in wild than farmed cervids. The prevalence is usually less than 1% in elk; however, it can be as high as 30% in concentrated populations of wild deer. Between 1996 and 1999, 4.7% of mule deer, 2% of white-tailed deer, and 0.5% of elk killed in northeastern Colorado and southeastern Wyoming were infected with the CWD prion overall, although there were “hot spots” where greater numbers of deer were infected. In Wisconsin, up to 13% of the male deer are infected in some areas. In contrast, the estimated prevalence in South Dakota in 2003 was 0.001% in white-tailed deer and no cases were reported in elk or mule deer. More than 97% of cases found during the surveillance of wild deer and elk are subclinical.

The prevalence of CWD in moose is unknown; however, moose tend to be solitary, which reduces the risk of transmission, and cases are probably rare. Whether moose become ill is unknown.

**Diagnosis**

**Clinical**

Chronic wasting disease should be suspected in cervids over the age of 16 months that have weight loss or chronic wasting, unusual behavior, neurologic signs, excessive salivation, polyuria/polydipsia, signs of aspiration pneumonia and/or unusual retention of the winter coat. In farmed herds, only one animal is usually affected at a time, but there may be a herd history consistent with CWD.

**Differential diagnosis**

Other neurologic diseases must be ruled out. The differential diagnoses include hemorrhagic disease (epizootic hemorrhagic disease and bluetongue) and meningeal worm (*Parelaphostrongylus tenuis*) infection.

Locoweed intoxication should also be considered in elk, but this disease has not been reported in deer.

**Laboratory tests**

Histological examination of the brain can be very helpful in diagnosis, but some animals in the early stages of the disease have few or no spongiform changes. Chronic wasting disease is usually diagnosed by detecting prions in the CNS and/or the lymphoid tissues. Prions can be found in areas of the brain that do not have spongiform changes. Immunohistochemistry (IHC) is considered to be the "gold standard" for diagnosis. Automated IHC staining is the official USDA test for surveillance in captive cervids. Immunoblotting (Western blotting) and rapid tests including enzyme-linked immunosorbent assays (ELISAs) and a rapid antigen-detection strip test are also used to screen cervids. In autolyzed brains, CWD may also be confirmed by finding characteristic prion fibrils called scrapie-associated fibrils (SAF) with electron microscopy; however, this test has low sensitivity. Two diagnostic methods under investigation are 1) assays that combine additional techniques with ELISAs to increase sensitivity, and 2) protein misfolding cyclic amplification, a new technique that detects tiny amounts of prions by their ability to convert PrPc (the normal cellular protein) into prions in vitro. Animal inoculation may be used to detect prions in special circumstances, but this technique is lengthy and labor intensive. Serology is not useful for diagnosis, as antibodies are not made against the CWD agent.

Confirmation of CWD is by immunohistochemistry, which can be combined with histological examination.

**Samples to collect**

Samples should be sent under secure conditions and only to authorized laboratories to prevent the spread of the disease. Although no human infections have been linked to CWD, there is a possibility that this disease could be zoonotic; samples should be collected and handled with all appropriate precautions.

CWD prions can be found in both the CNS and lymphoid tissues of cervids. In deer, prions can usually be found in the tonsils and retropharyngeal lymph nodes before they accumulate in the brain and before clinical signs appear. Approximately 10-15% of elk that have prions in the brain do not have prions in the lymphoid tissues; this occurs in less than 1% of deer.

Chronic wasting disease can be diagnosed in live animals, particularly deer, with tonsil biopsies. Prions are associated with the tonsilar follicles; one study found that more follicles were collected by the dorsolateral than the ventral-medial approach. Lymphoid biopsies are less useful in elk, which have only small amounts of prions in these tissues. The need for anesthesia and invasive procedures can limit the usefulness of antemortem testing.

Brain and lymphoid tissues should be collected at necropsy. Both unfixed (fresh) and formalin-fixed tissues...
should be taken. In the brain, the optimal site for diagnosis is the medulla oblongata at the level of the obex. Obex samples may be collected through the foramen magnum. Whole heads are sometimes submitted. In deer, prions can often be found in the retropharyngeal lymph nodes and tonsils before the brain; however, both lymphoid tissue and obex samples should be tested in elk. In a limited number of moose, prions have been detected in the brain (medulla oblongata), cervical spinal cord and lymphoid tissues including the retropharyngeal lymph node, palatine tonsil and submandibular lymph node. Fresh tissues should be kept cold and sent to the laboratory as soon as possible on wet ice or gel packs.

Prions can be detected in autolyzed samples; however, these samples are not ideal, as it can be difficult to determine whether the obex is represented in the sample.

**Treatment**

There is no treatment for chronic wasting disease.

**Recommended actions if chronic wasting disease is suspected**

**Notification of authorities**

Although chronic wasting disease is endemic in the U.S., it is a reportable disease in many states. All deaths must be reported in farmed cervid herds participating in the U.S. herd certification program, and samples must be submitted from these animals by a CWD-certified veterinarian or other authorized individual.

- Federal: Area Veterinarians in Charge (AVICS) www.aphis.usda.gov/animal_health/area_offices/

**Control**

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 that are negative for this disease. Voluntary and/or mandatory programs to control or manage CWD in farmed cervids, with eradication as the ultimate goal, have been established in the U.S. and Canada. Control programs are based on the identification of individual animals, fencing, restrictions on herd additions, and CWD testing of cervids that die on the farm or are slaughtered. In the U.S., herds can usually become certified after 5 years of participation; slaughter surveillance is no longer required after this time. A CWD monitored program, in which a percentage of the animals are tested each year, is also available in the U.S. Further details on these programs are available online at federal websites (see Internet Resources), as well as from individual states and provinces.

When CWD is found in a herd, the herd is usually quarantined. Herd and premises plans are developed and, in some cases, the herd is depopulated. Carcasses from CWD-infected animals cannot be used as food for humans or other animals and must be destroyed. Carcasses may be burned or buried, depending on local regulations. Korean authorities have attempted to eradicate CWD by slaughtering all imported deer, as well as indigenous deer that had been in contact with these deer or were born from them.

Controlling CWD is very difficult in wild cervids. Some states have culled their herds to reduce population density and decrease the spread of disease. Culling programs might be able to eradicate CWD from a limited area if it was introduced recently. Infected captive cervids should be kept from contact with wild cervids. Many states and provinces also have restrictions on the transportation of tissues from hunter-killed cervids in CWD endemic areas. These guidelines are available at the Chronic Wasting Disease Alliance website (see Internet Resources), state websites and other sources.

Decontamination of prion-contaminated tissues, surfaces and environments is difficult. These agents are highly resistant to most disinfectants (including formalin), heat, ultraviolet radiation and ionizing radiation, particularly when they are protected in organic material or preserved with aldehyde fixatives, or when the prion titer is high. Prions can bind tightly to some surfaces, including stainless steel and plastic, without losing infectivity. Prions bound to metal seem to be highly resistant to decontamination. Few effective decontamination techniques have been published. 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 2% available chlorine, has traditionally been recommended for equipment and surfaces. Surfaces should be treated for more than 1 hour at 20°C (68°F). Overnight disinfection is recommended for equipment. Cleaning before disinfection removes organic material that may protect prions. Recently, milder treatments including a phenolic disinfectant, an alkaline cleaner (KOH with detergents), and an enzymatic cleaner combined with vaporized hydrogen peroxide have been shown to inactivate scrapie and/or BSE prions. Their effectiveness against CWD prions has not been tested, but would probably be similar. These disinfectants may be useful for items that cannot withstand harsher decontamination procedures. Physical inactivation of prions can be carried out by porous load autoclaving at 134-138°C (273-280°F) for 18 minutes at 30 lb/in2. Autoclaving items in water is more effective than autoclaving without immersion. Dry heat is less effective; some prions can survive dry heat at temperatures as high as 360°C (680°F) for an hour. A combination of chemical and physical decontamination can be more effective than either procedure alone; chemical disinfection should be carried out first, then the items should be rinsed and autoclaved. Anecdotal evidence suggests that decontamination of contaminated facilities is very difficult.
Even the harshest combination of chemical and physical disinfection is not guaranteed to destroy all prions. In some experiments, a stainless-steel wire remained infectious after cleaning with sodium hydroxide and autoclaving.

**Public Health**

The emergence of variant Creutzfeldt Jakob disease in humans infected with the BSE prion has raised concerns about the zoonotic potential of other TSEs including chronic wasting disease.

Whether people are susceptible to CWD is not known. As of 2008, surveillance, investigation of suspicious cases of neurologic disease in humans and epidemiological studies have found no evidence that this disease is zoonotic. Molecular compatibility studies suggest that there is a significant species barrier and the CWD prion is not well adapted to infect humans. Nevertheless, the possibility that CWD is zoonotic cannot be ruled out at this time. Meat and other tissues, as well as lymphoid tissues and CNS, could be sources of exposure. Because prions have also been shown to be present in the blood and saliva of deer, no tissues from CWD infected cervids should be considered ‘safe’.

Hunters should check with their state wildlife agencies for current precautions and information on endemic areas. Hunters should consider having carcasses tested for CWD; information on this program is available from most state wildlife agencies. 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. Gloves should be worn when field-dressing a 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) may reduce the risk of exposure, but will not necessarily remove all prions. It may be prudent to avoid eating any tissues from untested cervids in endemic areas.

Veterinarians and laboratory workers should take standard precautions when conducting necropsies on CWD-suspects or handling tissues; BSL-2 is the recommended level of protection. Standard precautions include the use of protective clothing and the avoidance of penetrating injuries, contamination of abraded skin, and ingestion. A negative pressure laminar flow hood may be considered for some tissue manipulations. Because prions may be able to survive in the environment for years and are difficult to disinfect, precautions should be taken to avoid contamination of surfaces and equipment. Disposable plastic-coated paper sheets can be used to protect tables and other surfaces. Disposable instruments and work clothing can also be used. No vaccine is available.

**Internet Resources**

- Chronic Wasting Disease Alliance (CWDA) [http://www.cwdfed.org/](http://www.cwdfed.org/)

**References**

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*Link defunct as of 2008