Chronic Wasting Disease in Free-Ranging North American Cervids

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ABSTRACT: Chronic Wasting Disease (CWD) was first described in captive mule deer in a Colorado research facility in 1967 and subsequently classified as a transmissible spongiform encephalopathy in 1978. The first detection of CWD in a free-ranging population was in Colorado elk in 1981. During the 1990s, CWD was identified in free-ranging mule deer, white-tailed deer, and elk in Colorado and Wyoming. By 2000, CWD was considered a disease affecting free-ranging and captive cervids, with a limited distribution in several western states and western provinces in Canada. Following the outbreak of Bovine Spongiform Encephalopathy in Great Britain during the 1980s and resulting variant Creutzfeldt-Jakob disease in humans in the 1990s, CWD began to garner more attention. Surveillance for CWD increased in both captive and free-ranging cervids, and the disease was subsequently identified in numerous additional locations. Currently, CWD has been detected in either free-ranging or captive deer and elk in 14 states and 2 Canadian provinces. Most recently (2005), the disease was detected in free-ranging deer in New York, West Virginia, Kansas, and Alberta and in captive herds in New York. Across most of the geographic range where CWD has been detected, disease prevalence remains low. However, the disease has continued to spread from the initial foci where it was detected and continued to increase in prevalence. Management efforts to contain or eradicate CWD have not yet been successful, and in some local areas the disease has reached disconcerting levels.

KEY WORDS: cervids, chronic wasting disease, deer, elk, transmissible spongiform encephalopathy

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AGENT, TRANSMISSION, AND DIAGNOSES

Chronic wasting disease (CWD) (Williams and Young 1980) belongs to a family of diseases known as transmissible spongiform encephalopathies (TSEs) that affect both animals (sheep scrapie, bovine spongiform encephalopathy – BSE, transmissible mink encephalopathy – TME) and humans (a variant of Creutzfeldt-Jakob disease – vCJD, and Kuru). The causative agent of TSEs is likely an abnormal form of cellular proteins, called prions, which are consistently associated with the disease (Prusiner 1991). Prions, or proteinaceous infectious proteins, are relatively short proteins produced by all animals. While their function has yet to be completely elucidated, normal prions have a relatively short half-life because they are broken down within the body and eliminated or recycled. However, normal prions can be converted into a rogue, disease-associated isoform by contact with other abnormal prions within the body. These abnormal prions are highly resistant to degradation and tend to cluster into starch-like fibrils or plaques. This isoform of the prion protein is associated with neuronal damage associated with TSE disease.

Transmission in many TSE diseases (BSE, TME, vCJD, Kuru) has been linked to consumption of tissues containing infectious prions; when disease-causing prions are removed from the food chain, disease transmission is stopped. With CWD (and scrapie), disease transmission is not linked to contaminated food. Studies in captive mule deer (*Odocoileus hemionus*) and elk (*Cervus elaphus*) indicate that lateral transmission by direct contact and ingestion of abnormal prions is a likely mechanism for infection (Williams and Young 1992; Miller *et al.* 1998, 2000; Miller and Williams 2003). Indirect transmission from infected cervids to the environment, and then to susceptible cervids, is also suspected to be an important factor in transmission (Miller *et al.* 2004), but the mechanisms for indirect transmission and their significance in free-ranging cervids are not understood. In both cases, it is believed that infectious prions are shed via contaminated body fluids (e.g., saliva) or fecal material from infected animals and subsequently ingested by a susceptible animal. In addition, infected carcasses are a suitable source of infectious prions in the environment (Miller and Williams 2003). It does not appear that vertical transmission (doe to fawn) is an important component of CWD transmission (Gross and Miller 2001, Miller and Williams 2003, Grear *et al.* 2006). The effects of prion dose, genetic resistance, and prion strains on CWD transmission and disease progression are uncertain.

Immune responses associated with CWD are not evident, and natural resistance to infection has not been apparent (Williams *et al.* 2002). Variable susceptibility to scrapie has been associated with different genotypes in sheep, but genetic resistance to CWD has not been confirmed in most cervids (O'Rourke *et al.* 1999, Johnson *et al.* 2003). Recent studies in elk suggest either genetic resistance or differential incubation time associated with some genotypes (Hamir *et al.* 2006). However, almost all deer housed in research facilities contaminated with CWD agent eventually become infected (Williams and Young 1980). Clinical signs develop at ≥1.5 years after infection in wild mule deer (Williams *et al.* 2002) and include changes in behavior excessive salivation, periods of somnolence, and loss o body condition. Microscopic spongiform lesions an

detection of abnormal prion protein in the brain accompany clinical signs. No captive or wild cervid has ever recovered once clinical signs develop (Williams *et al.* 2002). Similarities between lesions, course of disease, and occurrence of interspecies transmission indicate that the same CWD agent can infect all 3 species (Williams *et al.* 2002). Currently, there are no known protection methods or vaccination to prevent CWD infection.

Diagnosis of CWD in cervid tissues using rapid enzyme linked immunosorbent assay (ELISA) methods is typically confirmed by the detection of abnormal prions in the brain, lymph nodes, or tonsils through immunohistochemistry (IHC) and/or the presence of spongiform lesions in the brain (Gavier-Widén *et al.* 2005). Accumulation in tonsils may occur as early as 1 month post exposure, and biopsied tonsil tissues have been used for ante-mortem CWD diagnoses in mule deer and white-tailed deer (*Odocoileus virginianus*) (Sigurdson *et al.* 1999, Williams *et al.* 2002, Wolfe *et al.* 2002). The recent development of highly sensitive transgenic mouse models has also been used to demonstrate the presence of infectious prions in deer muscle (Angers *et al.* 2006).

HOST RANGE AND DISTRIBUTION

CWD is the only infectious TSE that affects free-ranging cervid species including elk, mule deer, white-tailed deer (Miller *et al.* 2000), and it was recently discovered in wild moose (*Alces alces*) in Colorado. The disease was first recognized in captive cervids in the 1960s, and since 1981 in free-ranging cervids, but the actual length of time the disease has been present in North American cervids is unknown. Before 2000, CWD was primarily viewed as a disease affecting wild cervid populations in Colorado, Wyoming, and surrounding states. By 2004, CWD was found in free-ranging cervids in portions of Colorado, Nebraska, South Dakota, Wyoming, Saskatchewan, New Mexico, Illinois, Utah, and Wisconsin (Williams 2005). Since that time, CWD-infected cervids have also been reported from Alberta, New York, West Virginia, and Kansas. Currently, there is no scientific evidence that CWD has caused population declines in free-ranging deer or elk populations. However, computer simulations have shown that long-term declines are possible (Gross and Miller 2001). In addition, CWD prevalence has continued to rise in endemic areas and may soon reach levels where local populations cannot support hunting. At this time, it is difficult to ascertain whether CWD has spread to these new areas, or if disease has finally been detected in areas where it previously existed. The distribution of CWD in North America remains uncertain because adequate sampling and surveillance of free-ranging populations have not been conducted in most areas of the continent (Samuel *et al.* 2003).

Like other TSEs, CWD has the theoretical potential to infect other species of wildlife, domestic livestock, and humans. In CWD-affected areas, infectious carcasses or remains from harvest are likely scavenged by numerous species of native wildlife or domestic animals. Field and laboratory studies are currently underway to evaluate carcass decomposition, determine primary scavenging species, determine if CWD can infect other wildlife, and to understand the potential for interspecies transmission. In the absence of specific research studies, species that are known to contract a TSE should be investigated as potential hosts for CWD. Mink (*Mustela vison*), skunks (*Mephitis mephitis*), cats (*Felis catus*), raccoons (*Procyon lotor*), and small rodents are among common mammals that have demonstrated susceptibilities to TSEs (Williams 2000). Raccoons can develop TSE from intracerebral inoculation (injection of infectious material into the brain) with transmissible mink encephalopathy (TME) (Hamir *et al.* 2003*b*). Raccoons inoculated with mule deer CWD did not develop TSE, but raccoons developed TSE from inoculation with scrapie (Hamir *et al.* 2003*a*). Further testing of wildlife and domestic animals is currently being conducted to understand their potential susceptibility to CWD and whether susceptibility depends on the CWD host species (e.g., mule deer, white-tailed deer, elk).

At the current time, it appears that potential for natural transmission of CWD into domestic livestock is generally low. Domestic ruminants including cattle, sheep, and goats have resided in facilities with CWD-infected deer and elk and have not developed the disease (Williams 2005). While intracerebral inoculation has produced infection in cattle, long-term studies where CWD-positive deer have been housed with cattle have not resulted in transmission. Ongoing research in some domestic animals indicates possible susceptibility differences between CWD agents from different host species (A. N. Hamir, pers. commun.). Further research is needed to evaluate native and domestic species and to determine if susceptibility differences occur based on CWD host species.

Although many people have consumed venison from CWD-infected cervids, there is no current evidence that CWD has resulted in human disease (Belay *et al.* 2004, Qingzhong Kong *et al.* 2005). These studies have been based primarily on epidemiological monitoring of CJD rates or case studies of individuals consuming venison. However, some researchers have postulated that exposure in humans has not yet been sufficient to detect an increase in CJD prevalence. Cell-free conversion (test tube) studies have reported that CWD prions have caused human proteins to convert into disease-associated forms, but at a low rate. These studies have concluded there is a substantial species barrier to CWD infection in humans. Studies using humanized, transgenic mice have also concluded that humans are unlikely to develop infection from the consumption of CWD infected elk tissue (Qingzhong Kong *et al.* 2005). Although squirrel monkeys are susceptible to CWD by intracerebral inoculation with infected mule deer tissue, this species of primate is very permissive to TSE infections and may be a poor model for potential CWD infection in humans (Marsh *et al.* 2005). Other inoculation studies in non-human primates are currently in progress (Williams 2005). While the potential for human disease cannot be completely ruled out, the risk associated with consumption of venison is apparently quite low relative to risks associated with many day-to-day activities. Nevertheless, animals testing positive for CWD should not be consumed by humans or other animals (World Health Organization 2000).

DISEASE MANAGEMENT

A variety of management plans have been developed by agencies to deal with the presence or potential presence of CWD in wild deer and elk populations (Samuel *et al.* 2002). In general, these management goals include: 1) prevention of CWD, 2) control or containment of CWD, 3) elimination of CWD, and 4) monitoring for prevalence, distribution, and mortality of CWD in a population. These management goals are influenced by the extent and intensity of disease, as well as economic, social, and political factors. Big game hunting remains a multi-billion-dollar activity in the United States with more than 10 million hunters spending 150 million days hunting each year. Because CWD is a relatively new disease for which our scientific knowledge is generally limited, the best programs for CWD management have not been determined. This has reduced public acceptance of population reduction programs to manage the disease. Even in states where disease management has been attempted, CWD has continued to spread from its initial foci and/or continued to increase in prevalence.

Two characteristics of this disease make it particularly difficult to manage. First, empirical data indicate CWD transmission can occur at low deer densities. Thus, high levels of population reduction or complete removal of deer may be required to eradicate the disease. Information from Wyoming and Colorado suggests that simply containing CWD may require reducing cervid densities below 1-2 animals/km^2 of critical habitat (i.e., winter range) across large areas. Second, limited studies suggest infectious prions may persist in the environment for years. Therefore, in areas with high levels of environmental contamination, deer densities may need to be maintained at low levels for at least 5 to 10 years to ensure the disease is not introduced from the environment into re-established deer populations. Once CWD becomes established in wild populations, eradication is difficult; therefore, preventing establishment of new foci of disease must be seen as the primary objective of any CWD management program. Significant measures have been taken by many states and provinces to prevent movement of potentially CWD-infected cervids or transmissible material to new areas.

Many states have banned the practices of feeding deer and hunting deer over bait, which result in artificially enhanced rates of animal-to-animal contact. Artificial baiting and feeding areas provide means for prolonged continuous interactions among individuals. These unnatural aggregations of deer probably increase the likelihood of direct transmission among individuals (Williams *et al.* 2002, Spraker *et al.* 1997). Most wildlife experts agree that baiting and feeding of wildlife poses considerable risk for transmission of infectious disease, as the unnatural aggregations provide the potential for amplified CWD transmission through direct contacts and/or environmental contamination. Long-term feeding areas may pose an even more significant risk because of the resilience of the prion agent in the environment.

Where CWD is already established in wild populations, disease management objectives should consider reducing the prevalence of CWD to reduce levels of environmental contamination, reduce the rate of disease transmission, and reduce the probability of disease spread. Currently, appropriate management actions to achieve these objectives have not been determined; however, in most situations management will likely focus on cervid population reduction. This approach should consider in the area where the disease has been detected, as well as in a surrounding buffer area where infected animals are likely to migrate or disperse (Bollinger *et al.* 2004). In addition, specific strategies to cull animals showing clinical signs and to cull dispersing animals also could help to reduce spread. Surveillance programs in these buffer areas should be sufficient to detect CWD at extremely low levels, in order to identify potential new foci of disease.

The potential impacts and management strategies for CWD control in cervid populations remains controversial. Population models suggest that CWD could have a substantial long-term impact on affected populations (Gross and Miller 2001; J. R. Cary, Univ. of Wisconsin, unpubl. data). Although CWD can cause direct mortality of cervids, the long-term population effects of the disease are not well known. In addition, public concerns regarding potential domestic animal or human risk of contracting CWD can decrease the perceived value of wild cervids and affect hunter participation (Petchenik 2003), which increase the difficulty of managing high-density cervid populations. Currently, there is no evidence that CWD will spontaneously disappear or be controlled without management intervention (Gross and Miller 2001, Peterson *et al.* 2002). In contrast, there is demonstrated potential for significant expansion of the geographic range of the disease. Once established, the disease could be maintained through environmental contamination for an unknown period of time (Peterson *et al.* 2002, Miller *et al.* 2004).

Typically, management strategies involve surveillance to determine the prevalence and distribution of disease coupled with intensive culling of animals within the affected area (Williams *et al.* 2002, Nebraska Game and Parks Commission 2002, Bartelt *et al.* 2003). Culling strategies to reduce prevalence or eradicate CWD by a general reduction in cervid densities have assumed that CWD transmission is density dependent (Schauber and Wolf 2003) and homogeneous among different groups of animals. As further information is obtained on the specifics of CWD transmission among wild cervids, it may be possible to develop management strategies that are targeted at infected animals and reduce transmission rates. Further research is needed to understand the impact of CWD on free-ranging cervid populations, improve surveillance and management strategies, and determine whether CWD transmission is density or frequency dependent.

The best source for additional information on Chronic Wasting Disease is the CWD Alliance (www.cwd-info.org), which provides links to state, federal, and tribal web sites concerned with CWD, research findings, links to popular articles, and regulatory and policy documents. An overview of issues related to CWD surveillance is provided in "Surveillance Strategies for Detecting Chronic Wasting Disease in Free-Ranging Deer and Elk: Results of a CWD Surveillance Workshop" (Madison,

WI, December 10-12, 2002) and is available at: http://www.nwhc.usgs.gov/research/chronic_wasting/CWD_Surveillance_Strategies.pdf.

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