CHRONIC WASTING DISEASE: IMPLICATIONS AND CHALLENGES FOR WILDLIFE MANAGERS

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Abstract

Chronic wasting disease (CWD) is a transmissible spongiform encephalopathy (TSE) of deer (*Odocoileus* spp.) and Rocky Mountain elk (*Cervus elaphus nelsoni*). Other TSEs include important diseases of domestic animals (scrapie, bovine spongiform encephalopathy) and rare fatal diseases of humans (Creutzfeldt-Jakob disease and variant Creutzfeldt-Jakob disease); the bovine spongiform encephalopathy agent apparently causes variant Creutzfeldt-Jakob disease. In recent years intense interest in CWD has developed because of its similarities to the other TSEs; the media focus about these diseases;

concerns about public health; unknowns about transmission and host range of the CWD agent; presence of CWD in commercially owned elk; and questions about its impact on free-ranging deer and elk populations. Consequently, wildlife managers are faced with developing programs for addressing CWD. Implications of CWD are not entirely known at this time and probably will change as more is learned. At a minimum, we know that CWD is a fatal, contagious disease of the mature reproductive segment of deer and elk populations. At the other end of the spectrum, although there is currently no evidence that this occurs, it is possible that CWD could infect domestic livestock or even humans. Should this be the case, there could be tremendous impact on how cervids are managed in areas where CWD is endemic. Where CWD is not known to occur, managers should and are developing surveillance programs and regulations that prevent or reduce the likelihood that CWD will be introduced into their jurisdictions. In the known CWD-endemic area, management actions are aimed at surveillance to assess prevalence and geographic distribution and changes in these over time; limiting expansion of the CWD endemic area; and developing techniques for controlling and ultimately eradicating CWD. Programs for addressing the challenges of CWD management will require interagency cooperation, commitment of funds and personnel, and applied research.

Introduction

Chronic wasting disease (CWD) is a transmissible spongiform encephalopathy (TSE) of cervids. The TSEs are grouped together because of similarity in clinical features, pathology, and presumed etiology; the infectious agents are hypothesized to be prions (infectious proteins without associated nucleic acids) (Prusiner 1999). Scrapie of domestic sheep and goats, bovine spongiform encephalopathy (BSE) of cattle, and transmissible mink encephalopathy of farmed mink (*Mustela vison*) are TSEs of domestic animals. Several rare fatal diseases of humans are also TSEs; Creutzfeldt-Jakob disease (CJD) occurs worldwide and variant Creutzfeldt-Jakob disease is associated with the agent of BSE where it occurs in cattle, including the United Kingdom and parts of continental Europe. Since the appearance of BSE in the mid-1980s and, especially since the 1996 announcement of an apparent relationship between

BSE and variant CJD (Will et al. 1996), there has been considerable media, public, and animal and human health agency interest in TSEs. Consequently, CWD is a disease of increasing concern for wildlife managers both in CWD-endemic areas and across North America. Many biological features of CWD pose significant challenges for wildlife managers attempting to control or eradicate the disease. Perhaps even greater challenges are those associated with balancing complex and often competing and conflicting interests of the general public, sportsmen, the game farming industry, traditional livestock industries, and many state and federal animal health and public health agencies. This is a short review of the biological features of CWD and strategies being used for its control and management.

History of Chronic Wasting Disease

Chronic wasting disease (CWD) has been known as a clinical syndrome of mule deer (*Odocoileus hemionus*) for more than 30 years (Williams and Young 1980); modeling suggests the disease may have been present in free-ranging populations of mule deer for more than 40 years (Miller et al. 2000). Key events in the chronology of CWD are shown in Table 1. Only three species of the family Cervidae are known to be naturally susceptible to CWD: mule deer, white-tailed deer (*Odocoileus virginianus*), and Rocky Mountain elk (*Cervus elaphus nelsoni*), though it is very likely that other subspecies of *C. elaphus* are susceptible to CWD. Susceptibility of other cervids to CWD is not known. Cattle and other domestic livestock appear to be resistant to natural infection; to date, only three of 13 cattle have become infected with the CWD agent following experimental intracerebral inoculation (Hamir et al. 2001), although this and other experimental studies begun in 1997 are not yet completed (Williams et al., unpublished data).

The origin of CWD is not known and it may never be possible to definitively determine how or when CWD arose. Though of academic interest, determining the origin is probably not very important from a management perspective; nonetheless, speculation continues. Scrapie, a TSE of domestic sheep, has been recognized in the United States since 1947, and it is possible that CWD was derived from scrapie. Arguments can be made both for and against this hypothesis. It is possible, though never proven, that deer came into contact with scrapie agent either on shared pastures or in captivity somewhere along the front range of the Rocky Mountains, where high levels of sheep grazing occurred in the early 1900s. In addition, in vitro models suggest there is less of a species barrier to interspecies TSE transmission between deer, elk, and sheep than between these cervids and either cattle or humans (Raymond et al. 2000). However, CWD has never been identified in other areas of North America or other parts of the world where cervids and domestic sheep with scrapie must have co-mingled. Strain typing experiments determined that CWD is not like known scrapie strains (Bruce et al. 2000), though direct comparisons with North American scrapie strains has not been conducted. Experimental transmission of CWD to a domestic goat by intracerebral inoculation had a prolonged incubation (Williams and Young 1992); shorter incubation would be expected with scrapie strains in goats. Experimental scrapie in cattle (Cutlip et al. 1994; Cutlip et al. 1997) and lesions of CWD in cattle are quite different (Hamir et al. 2001).

It may be possible that CWD is a spontaneous TSE that arose in deer in the wild or in captivity and has biological features promoting transmission to other deer and elk. The majority of human CJD cases are thought to be spontaneous (Gajdusek 1996) and associated with conformational change in a normal cellular protein (PrP^C) to the abnormal disease associated protease resistant protein (PrP^{res}) considered by many to be infectious agents of the TSEs. Occurrence of spontaneous CJD is approximately 1 per 1 million population per year. Spontaneous CWD may have happened in deer though it is difficult to see how this could be proven.

Clinical Signs

Chronic wasting disease-affected deer and elk show loss of body condition and changes in behavior. The clinical disease is often more subtle and prolonged in elk than in deer. Affected animals may walk repetitive courses; they may show subtle ataxia and wide based stance; subtle head tremors occur in some animals; they may be found near water sources or in riparian areas; they may have periods of somnolence; and they may carry their head and ears lowered. Chronic wasting disease affected animals continue to eat but amounts of feed consumed are reduced, leading to gradual loss of body condition. Excessive drinking and urination are common in the terminal stages because of specific lesions in the brain. Many animals in terminal stages of CWD have excessive salivation and drooling; this may result in wetting of the hairs of the chin and neck. Death is inevitable once clinical disease occurs.

The clinical course of CWD varies from a few days to approximately a year, with most animals surviving from a few weeks to several months. While a protracted clinical course is typical, occasionally acute death may occur; this may be more common in the wild than in the relative security of captivity. Aspiration pneumonia is a common finding at postmortem examination of terminal CWD cases and may confuse the diagnosis if the brain is not examined. Aspiration pneumonia presumably is due to difficulty swallowing, hypersalivation, and inhalation of foreign material into the lungs. Thus the brain should be examined for evidence of CWD on every prime age cervid that dies with pneumonia.

Diagnosis

Clinical signs of CWD alone are not diagnostic and definitive diagnosis is based on examination of the brain for spongiform lesions and/or accumulation of the CWD associated protease resistant protein (PrP^{CWD}) in brain and lymphoid tissues by immunohistochemistry. This test is based on use of monoclonal antibodies and chromogens to detect accumulation of PrP^{CWD} in various tissues. The parasympathetic vagal nucleus in the dorsal portion of the medulla oblongata at the obex (Figure 1) is the most important site to examine for diagnosis of CWD (Williams and Young 1993; Peters et al. 2000) because of its early involvement following infection. It is critically important that the correct portion of the brain be sampled for a meaningful test. The segment of the medulla oblongata required for testing can be easily and swiftly removed from the brain through the foramen magnum (with practice) and the specimen appropriately preserved (the obex in 10% buffered formalin and remaining brain frozen).

Demonstration of PrP^{CWD} in lymph nodes and tonsil of mule deer early in incubation (Sigurdson et al. 1999) provides a reliable means of antemortem and preclinical diagnosis of CWD (Miller and Williams submitted; Wolfe et al. submitted). However, due to differences in pathogenesis of CWD in elk, sampling lymphoid tissue in elk does not appear to be sensitive enough to use as a reliable antemortem diagnostic test.

Several laboratory tests developed for BSE are being evaluated for use in CWD diagnostics. If these tests are determined to be adequately sensitive and specific in subclinically affected cervids they may provide for more rapid testing than is currently possible using immunohistochemistry.

Epidemiology

Chronic wasting disease is both transmissible and infectious, but most details of its transmission remain to be determined. In contrast to BSE (Wilesmith et al. 1988), CWD is not a foodborne disease associated with rendered ruminant meat and bonemeal. Instead, observations of CWD among captive deer and elk provide strong evidence of lateral transmission (Williams and Young 1992; Miller et al. 1998; Miller et al. 2000) which is more similar to scrapie (Hoinville 1996); experimental and epidemic modeling data support these anecdotal observations (Miller et al. 2000; Gross and Miller 2001; Miller, unpublished data). Maternal transmission may occur, but appears to be relatively rare and cannot explain most cases where complete epidemiologic data are available (Miller et al. 1998; Miller et al. 2000). Some interspecies transmission probably occurs among the three natural host species; suspected transmission from mule deer to elk, mule deer to white-tailed deer, and elk to mule deer and white-tailed deer has been observed.

The presumed CWD agent (PrP^{CWD}) has been demonstrated by immunohistochemistry in various lymphoid tissues, including those of the digestive tract (e.g., tonsil, Peyer's patches, and mesenteric lymph nodes) (Sigurdson et al. 1999; Spraker et al. 2002; Miller and Williams submitted). These distribution patterns suggest that PrP^{CWD} may be shed through the alimentary tract. Because TSE agents are extremely resistant in the environment (Brown and Gajdusek 1991), transmission may be both direct and indirect. Concentrating deer and elk in captivity or by artificial feeding probably increases the likelihood of direct and indirect transmission between individuals. Contaminated pastures appear to have served as sources of infection in some CWD epidemics (Miller et al. 1998; E. S. Williams et al., unpublished data; M.W. Miller, unpublished data);

similar phenomena have been suspected in some outbreaks of sheep scrapie (Greig 1940; Palsson 1979; Andreoletti et al. 2000). The apparent persistence of PrP^{CWD} in contaminated environments represents a significant obstacle to eradication of CWD from either farmed or free-ranging cervid populations.

The overall duration of CWD infection (time from exposure to end-stage clinical disease) has been difficult to determine in natural cases -- without clear knowledge of when animals become infected, it is impossible to accurately determine the overall course of disease. Experimental CWD challenge studies based on single-dose oral exposure to infectious brain tissue have yielded some insights into disease course; however, because the course of infection appears to be inversely related to exposure dose (i.e., greater exposure results in shorter duration), experimental data probably underestimate time frames for natural infections. Experimentally, minimum incubation (time from exposure to onset of clinical disease) was about 15 months and mean time from oral infection to death was about 23 months (range 20–>25 months) in mule deer (E. S. Williams and M. W. Miller, unpublished data); the range of incubation observed in orally infected elk was approximately 12–34 months (E. S. Williams et al., unpublished data). The maximum disease course is not known, but can exceed 25 months in experimentally-infected deer and 34 months in elk. Duration is less certain in naturally-occurring cases. The youngest animal diagnosed with clinical CWD was 17 months old, suggesting 16-17 months may be the minimum natural incubation period. Among deer and elk residing in facilities with a long history of CWD, most natural cases occur in 2-7 year-old animals; however, deer have lived >7 years in heavily infected facilities without succumbing to CWD and elk >15 years of age have succumbed to CWD. It is not known when during the course of infection an animal may become infectious, but it appears likely that PrP^{CWD} shedding is progressive through the disease course; epidemic models suggest shedding probably precedes onset of clinical disease in both deer and elk (M. W. Miller, unpublished data).

Chronic wasting disease can reach remarkably high prevalence in captive cervid populations. In one infected research facility, more than 90% of mule deer resident for >2 years died or were euthanized while suffering from CWD (Williams and Young 1980). Recently, high CWD prevalence (about 50%) has been demonstrated via immunohistochemistry in white-tailed deer confined in association with an infected Nebraska elk farm (B. Morrison, personal communication: 2002). Among captive elk, CWD was the primary cause of adult mortality (five of seven, 71%; four of 23, 23%) in two research herds (Miller et al. 1998) and high prevalence (59%) was detected by immunohistochemistry in a group of 17 elk slaughtered from an infected farm herd (Peters et al. 2000).

To estimate prevalence in infected free-ranging populations, tissues from deer and elk harvested by hunters in CWD-endemic areas have been collected and examined at random (Miller et al. 2000). Within endemic areas, prevalence of preclinical CWD, based on immunohistochemistry for PrP^{CWD}, has been estimated at <1-15% in mule deer and <1% in elk (Miller et al. 2000). Modeled CWD epidemics failed to achieve a steady-state equilibrium in infected deer populations, suggesting that CWD may lead to local extinctions of infected deer populations if left unmanaged (Gross and Miller 2001).

Distribution

Among captive cervid herds, CWD distribution has been determined through a combination of surveillance and epidemiologic investigations (Figure 2), and is probably underestimated at present. Chronic wasting disease in free-ranging cervids occurs in contiguous areas of Wyoming, Colorado (Miller et al. 2000) and Nebraska; this is considered the core endemic area for CWD (Figure 2). Distribution of CWD in free-ranging deer and elk has been determined primarily through necropsy and examination of tissues from animals showing clinical signs suggestive of CWD (clinically targeted surveillance); this is an efficient approach for detecting new foci of infection (Miller et al. 2000). With the exception of cases reported from Saskatchewan in mule deer and from northwestern Nebraska in white-tailed deer and mule deer, no CWD-infected free-ranging cervids have been detected outside the contiguous Wyoming-Colorado-Nebraska endemic area.

Control Strategies

No treatment is available for animals affected with CWD. Once clinical signs develop, CWD is invariably fatal. Affected animals that develop pneumonia may respond temporarily to treatment with antibiotics, but ultimately the outcome is still fatal. Similarly, no vaccine is available to prevent CWD infection in deer or elk. It follows that controlling CWD is problematic. Long incubation periods, subtle early clinical signs, absence of a reliable antemortem diagnostic tests, extremely resistant infectious agent, possible environmental contamination, and incomplete understanding of transmission all constrain options for controlling or eradicating CWD.

In captive facilities, management options currently are limited to quarantine or depopulation of CWD-affected herds. Two attempts to eradicate CWD from cervid research facilities failed; the causes of these failures were not determined, but residual environmental contamination following depopulation and/or facility clean-up was likely in both cases (Williams and Young 1992; Miller et al. 1998). Attempts to eliminate CWD from farmed elk populations are more recent, and consequently the efficacy of these attempts remains uncertain. Whether contaminated environments can ever be completely disinfected remains questionable. Until effective cleaning and disinfection procedures are identified, captive cervids should not be reintroduced into commercial facilities where CWD has occurred; moreover, free-ranging cervids also should be excluded from previously-infected premises. Establishment of free-ranging reservoirs of infection in the vicinity of infected game farms, as exemplified by probable cases in Saskatchewan and Nebraska, could severely impair attempts at eradication from captive facilities. Inherent difficulties in managing infected herds and premises underscore the need for aggressive surveillance to prevent movements of infected animals in commerce.

Managing CWD in free-ranging animals presents even greater challenges. Long-term, active surveillance programs to monitor CWD distribution and prevalence have been instituted in the endemic area to determine the extent of the endemic area and to assist in evaluating both temporal changes and effects of management intervention. Management programs established to date focus on containing CWD and reducing its prevalence in localized areas (Miller and Kahn 1999; Colorado Division of Wildlife 2001) Ultimate management goals vary among affected states and provinces. In Saskatchewan and Nebraska where CWD may not yet be endemic, eradication appears to be the ultimate goal for CWD management. In contrast, wildlife managers in Colorado and Wyoming have refrained from committing to eradication because it appears unattainable in their situations (Colorado Division of Wildlife 2001).

A variety of specific strategies for managing CWD in free-ranging wildlife have been adopted in affected jurisdictions. Translocating and artificially feeding cervids in endemic areas have been banned in attempts to limit range expansion and decrease transmission. Selective culling of clinical suspects has been practiced throughout the endemic area of Colorado and Wyoming for a number of years, but this approach alone has proven insufficient to reduce prevalence in affected populations. Localized population reduction in an area of high CWD prevalence has been undertaken in Colorado as a management experiment, but efficacy remains to be determined. Although it seems intuitive that lowered deer and elk densities should reduce both transmission and likelihood of emigration by affected animals to adjacent areas, historic migration patterns and social behaviors characteristic of some deer and elk populations may diminish the effectiveness of wholesale density reduction in controlling CWD. Models of CWD epidemic dynamics suggest early, aggressive intervention via selective culling or more generalized population reduction show the greatest promise of preventing new endemic foci from being established (Gross and Miller 2001); unfortunately, surveillance limitations (both cost and sensitivity) may delay detection of newly infected free-ranging populations for a decade or more after CWD has been introduced (Miller et al. 2000). In both Nebraska and Saskatchewan, aggressive reductions of deer numbers in newly-identified endemic foci have been undertaken in attempts to eliminate CWD from these areas. The recent development of tonsil biopsy as an antemortem test for CWD in deer might aid control efforts under some conditions, but large-scale applications to free-ranging populations seem impractical (Wolfe et al. submitted).

Public Health Concerns

No cases of human prion disease have been associated with CWD (World Health Organization 2000; Belay et al. 2001; Food and Drug Administration Transmissible Spongiform Encephalopathy Advisory Committee 2001). Contrary to a widely distributed story that recently circulated in the popular press, none of three “young hunters” diagnosed with CJD were connected epidemiologically to CWD exposure (Belay et al. 2001). The tendency toward a natural “species barrier”reducing human susceptibility to CWD and other prion diseases has been demonstrated by in vitro studies; in those studies, PrP^{CWD} inefficiently converted human PrP^{C} to the abnormal isoform as compared to homologous PrP^{CWD} to cervid PrP^{C} conversions. Cervid

PrP^{CWD} to human PrP^{C} conversions were essentially equivalent to conversions of human PrP^{C} by scrapie and BSE PrP^{res} (Raymond et al. 2000). However, lingering uncertainty about interpreting these data and assessing any potential risk that CWD may pose to humans is fostered by differing experiences with two more common animal TSEs. Although there is a long history of human exposure to scrapie through handling and consuming sheep tissues, including brain, there is no evidence that this presents a risk to human health. In contrast, massive exposure (Ghani et al. 2000) of British and perhaps other European citizens to the BSE agent resulted in approximately 106 deaths due to variant Creutzfeldt-Jakob disease as of February 2002 (The UK Creutzfeldt-Jakob Disease Surveillance Unit University of Edinburgh 2002).

In the absence of complete information on risk, and in light of similarities of animal and human TSEs, public health officials and wildlife management professionals recommend that hunters harvesting deer and elk in the endemic area, as well as meat processors and taxidermists handling cervid carcasses, should take some common sense measures to avoid exposure to the CWD agent and to other known zoonotic pathogens (Table 2). Because TSE agents have never been demonstrated in skeletal muscle (Spraker et al. 2002), boning game meat is recommended as an effective way to further reduce the potential for exposure. Raw velvet antler, a product unique to the farmed cervid industry, may deserve further evaluation for presence of PrP^{CWD} in order to preserve markets for this commodity.

Management Implications

Where it occurs, CWD in captive and free-ranging cervids represents serious management problems. Captive populations are quarantined, thus limiting use and value of infected or exposed animals. Indemnity for depopulated cervids has been made available only recently in the US; in Canada, the magnitude of infection in farmed elk herds detected thus far has cost the Canadian government over C$30 million in indemnity and clean-up funds (United States Animal Health Association 2001; G. Luterbach, personal communication: December 2001). Guidelines for management of captive herds with CWD are being developed by state and provincial animal health officials. A national program is nearing adoption in Canada, and a similar program is currently under review in the United States (United States Department of Agriculture 2001). Spillover of CWD into local free-ranging cervid populations may have occurred in two locations; further spillover could establish more endemic foci, thereby impairing long-term viability of both cervid farming and wildlife management in those areas.

Implications for free-ranging populations of deer and elk may be even more significant. Agencies do not translocate deer and elk from CWD endemic areas. Ongoing surveillance programs are expensive and draw resources from other wildlife management needs. Perhaps most important, impacts of CWD on population dynamics of deer and elk are presently unknown. Modeling suggests that CWD could substantially harm infected cervid populations by lowering adult survival rates and destabilizing long-term population dynamics (Gross and Miller 2001). Ultimately, public and agency concerns and perceptions about human health risks associated with all TSEs may erode participation in sport hunting in the endemic area, and also may have dramatic influence on management of free-ranging cervid herds where CWD is endemic. It follows that responsible wildlife management and animal health agencies should continue working to understand and limit distribution and occurrence of CWD in free-ranging and farmed cervids.

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Table 1. Chronology of significant events in the history of chronic wasting disease (CWD).

Year	Event
Late 1960s	first recognition of a clinical syndrome termed "chronic wasting disease" in captive mule deer in Colorado
1977/1978[a]	diagnosis of CWD in mule deer as a spongiform encephalopathy
1978/1979[a]	diagnosis of CWD in captive mule deer and black-tailed deer in Wyoming
1979	diagnosis of CWD in captive Rocky Mountain elk

late 1970s	diagnosis of spongiform encephalopathy in captive mule deer in a zoo in Ontario (CWD did not persist in this location)
1980	first published report of CWD in captive mule deer
1981	diagnosis of CWD in free-ranging Rocky Mountain elk in Colorado
1982	first published report of CWD in Rocky Mountain elk
1983	start of hunter-harvest surveillance for CWD

1985	diagnosis of CWD in free-ranging mule deer
1990	diagnosis of CWD in free-ranging white-tailed deer
1992	first published report of CWD in free-ranging cervids
1996	diagnosis of CWD in game farm elk in Saskatchewan
1997	diagnosis of CWD in game farm elk in South Dakota

2000/2001[a]	diagnosis of CWD in free-ranging mule deer in Saskatchewan, possibly associated with CWD affected elk farm
2000/2001[a]	diagnosis of CWD in free-ranging mule deer in Nebraska contiguous with the CWD endemic area of Colorado and Wyoming
2001	extensive depopulation of game farm elk in Saskatchewan due to CWD
2001	diagnosis of CWD in an elk imported from Canada to Korea in 1997
2001	declaration of a USDA animal emergency because of CWD in game farm elk

2002	diagnosis of CWD in free-ranging deer associated with an affected game farm in Nebraska

[a]Year samples collected/year diagnosis made.

Table 2. Recommendations for deer and elk harvested in the chronic wasting disease endemic area.

	Recommendations
During the hunt	harvest only animals that look and behave normally
During dressing	wear latex or rubber gloves
	avoid direct contact with the brain and spinal cord
	dispose of head (if not required to remain attached to carcass) or submit chilled head for CWD testing at a veterinary diagnostic laboratory[a]
	discard superficial lymph nodes with the hide and deep lymph nodes and spleen with the viscera
	use strong household bleach solution for cleaning knives and saws

During processing	avoid contamination of meat with nervous tissue
	debone the meat and discard[b] the vertebrae and head (or submit for testing)
	use strong household bleach solution for cleaning knives, saws, and cutting boards or tables

[a] The World Health Organization, Centers for Disease Control and Prevention, and state public health departments recommend that meat from CWD test positive deer and elk be discarded and not consumed by humans or other animals.

[b] Dispose of bones and head by incineration, deep burial, or in a sanitary landfill.

Figures

Figure 1. Diagram showing the correct portion of the brain needed for CWD testing by immunohistochemistry. The obex region should be fixed in 10% buffered formalin and the other portion of brain frozen.

Figure 2. Known geographic distribution of chronic wasting disease (CWD). A. Captive, commercially owned deer and elk. Circles indicate affected herds depopulated, quarantined, or released from quarantine without depopulation as of January 2002. The numbers refer to numbers of affected herds in Saskatchewan (40), South Dakota (6), and northeastern Colorado/western Nebraska (10), and the black lines and arrows indicate known movement of elk among affected farms. B. Free-ranging deer and elk. The outlines show the core CWD endemic area (Colorado, Wyoming, and Nebraska) and foci of CWD in Saskatchewan and Nebraska.