CHRONIC WASTING DISEASE: IMPLICATIONS AND CHALLENGES FOR WILDLIFE MANAGERS


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). 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, 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; modeling suggests the disease may have been present in free-ranging populations of mule deer for more than 40 years. 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, although this and other experimental studies begun in 1997 are not yet completed.

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. 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, 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; shorter incubation would be expected with scrapie strains in goats. Experimental scrapie in cattle and lesions of CWD in cattle are quite different.

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 and associated with conformational change in a normal cellular protein (PrPC) to the abnormal disease associated protease resistant protein (PrPres) 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.

Key events in the chronology of CWD are shown in the CWD Timeline

Clinical Signs

Clinical Features:

- Adults: 17 months to >15 years
- Most 3-5 years
- Sex: males, females
- No strict seasonality
- Clinical duration:
  - days to >1 year, usually months
  - Incubation period: min: ~17 months, max: unknown

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 (PrPCWD) in brain and lymphoid tissues by immunohistochemistry. This test is based on use of monoclonal antibodies and chromogens to detect accumulation of PrPCWD in various tissues. The parasympathetic vagal nucleus in the dorsal portion of the medulla oblongata at the obex is the most important site to examine for diagnosis of CWD 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).

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Photo Courtesy of Wyoming Game and Fish Department

Demonstration of PrPCWD in lymph nodes and tonsil of mule deer early in incubation provides a reliable means of antemortem and preclinical diagnosis of CWD. 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, 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 which is more similar to scrapie; experimental and epidemic modeling data support these anecdotal observations. Maternal transmission may occur, but appears to be relatively rare and cannot explain most cases where complete epidemiologic data are available. 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 (PrPCWD) 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). These distribution patterns suggest that PrPCWD may be shed through the alimentary tract. Because TSE agents are extremely resistant in the environment,
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; similar phenomena have been suspected in some outbreaks of sheep scrapie. The apparent persistence of PrPCWD 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; the range of incubation observed in orally infected elk was approximately 12–34 months. 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 PrPCWD shedding is progressive through the disease course; epidemic models suggest shedding probably precedes onset of clinical disease in both deer and elk.

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. Recently, high CWD prevalence (about 50%) has been demonstrated via immunohistochemistry in white-tailed deer confined in association with an infected Nebraska elk farm. 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.

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. Within endemic areas, prevalence of preclinical CWD, based on immunohistochemistry for PrPCWD, has been estimated at <1-15% in mule deer and <1% in elk. 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.

Distribution
Among captive cervid herds, CWD distribution has been determined through a combination of surveillance and epidemiologic investigations, and is probably underestimated at present. Chronic wasting disease in free-ranging cervids occurs in contiguous areas of Wyoming, Colorado and Nebraska; this is considered the core endemic area for CWD. 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. Since 2000, CWD has been detected in free-ranging cervids in several additional states (see Map and Frequently Asked Questions - Where Does CWD Occur?).
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 ante mortem 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. 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. 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.

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; 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. 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 ante mortem test for CWD in deer might aid control efforts under some conditions, but large-scale applications to free-ranging populations seem impractical.

Public Health Concerns
No cases of human prion disease have been associated with CWD. 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. 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, PrPCWD inefficiently converted human PrPC to the abnormal isoform as compared to homologous PrPCWD to cervid PrPC conversions. Cervid PrPCWD to human PrPC conversions were essentially equivalent to conversions of human PrPC by scrapie and BSE PrPres. 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 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.

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. Because TSE agents have never been demonstrated in skeletal muscle, 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 PrPCWD 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. 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. Spillover of CWD into local free-ranging cervid populations may have occurred in some 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. 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.
For more information on Chronic Wasting Disease Dr. Scott Wright at 608-270-2460, or Paul Slota, at 608-270-2420, USGS, National Wildlife Health Center

Distribution of sections from which CWD samples were obtained from 1 April 2003 to 20 Jan 2004.