

Epidemiology of Chronic Wasting Disease in Captive White-Tailed and Mule Deer

Authors: Miller, Michael W., and Wild, Margaret A.

Source: Journal of Wildlife Diseases, 40(2) : 320-327

Published By: Wildlife Disease Association

URL: <https://doi.org/10.7589/0090-3558-40.2.320>

BioOne Complete (complete.BioOne.org) is a full-text database of 200 subscribed and open-access titles in the biological, ecological, and environmental sciences published by nonprofit societies, associations, museums, institutions, and presses.

Your use of this PDF, the BioOne Complete website, and all posted and associated content indicates your acceptance of BioOne's Terms of Use, available at www.bioone.org/terms-of-use.

Usage of BioOne Complete content is strictly limited to personal, educational, and non - commercial use. Commercial inquiries or rights and permissions requests should be directed to the individual publisher as copyright holder.

BioOne sees sustainable scholarly publishing as an inherently collaborative enterprise connecting authors, nonprofit publishers, academic institutions, research libraries, and research funders in the common goal of maximizing access to critical research.

Epidemiology of Chronic Wasting Disease in Captive White-Tailed and Mule Deer

Michael W. Miller^{1,3} and Margaret A. Wild^{1,2} ¹ Colorado Division of Wildlife, Wildlife Research Center, 317 West Prospect Road, Fort Collins, Colorado 80526-2097, USA; ² Current address: National Park Service, Biological Resource Management Division, 1201 Oak Ridge Drive, Suite 200, Fort Collins, Colorado 80525, USA; ³ Corresponding author (email: mike.miller@state.co.us)

ABSTRACT: The natural occurrence of chronic wasting disease (CWD) in a 1993 cohort of captive white-tailed deer (*Odocoileus virginianus*) afforded the opportunity to describe epidemic dynamics in this species and to compare dynamics with those seen in contemporary cohorts of captive mule deer (*O. hemionus*) also infected with CWD. The overall incidence of clinical CWD in white-tailed deer was 82% (nine of 11) among individuals that survived >15 mo. Affected white-tailed deer died or were killed because of terminal CWD at age 49–76 mo ($\bar{x}$ =59.6 mo, SE=3.9 mo). Epidemic dynamics of CWD in captive white-tailed deer were similar to dynamics in mule deer cohorts. Incidence of clinical CWD was 57% (4/7) among hand-raised (HR) and 67% (4/6) among dam-raised (DR) mule deer; affected HR mule deer succumbed at 64–86 mo of age ($\bar{x}$ =72 mo; SE=5 mo), and affected DR mule deer died at age 31–58 mo ($\bar{x}$ =41.3 mo; SE=6.1 mo). Sustained horizontal transmission of CWD most plausibly explained epidemic dynamics, but the original source of exposures could not be determined. Apparent differences in mean age at CWD-caused death among these cohorts may be attributable to differences in the timing or intensity of exposure to CWD, and these factors appear to be more likely to influence epidemic dynamics than species differences. It follows that CWD epidemic dynamics in sympatric, free-ranging white-tailed and mule deer sharing habitats in western North American ranges also may be similar.

Key words: Chronic wasting disease, epidemiology, mule deer, *Odocoileus hemionus*, *Odocoileus virginianus*, prion, transmissible spongiform encephalopathy, white-tailed deer.

Epidemics of chronic wasting disease (CWD), a prion disease of North American cervids, were originally described in captive mule deer (*Odocoileus hemionus*) and elk (*Cervus elaphus nelsoni*) (Williams and Young, 1980, 1982, 1992; Miller et al., 1998). The first epidemics were recognized in wildlife research facilities in north-central Colorado and southeastern

Wyoming. Subsequent field investigations revealed cases of CWD in free-ranging cervids in these same areas (Williams and Young, 1992; Spraker et al., 1997; Miller et al., 2000). Although the vast majority of free-ranging cases were diagnosed in mule deer and elk, cases of CWD also were encountered in white-tailed deer (*O. virginianus*). Because the prevalence of CWD in free-ranging white-tailed deer was remarkably high in some locations, the smaller number of cases was regarded as reflecting the relative scarcity of white-tailed deer in these areas rather than innate species resistance to CWD (Miller et al., 2000). The recent discovery of CWD in both free-ranging and captive white-tailed deer in the upper midwestern United States (Williams et al., 2002; Joly et al., 2003) suggests that epidemics can arise in white-tailed deer populations in the absence of sympatric mule deer or elk populations.

The epidemic dynamics of CWD have not been described in white-tailed deer. This species was absent from affected research facilities during the 1960s–80s, when epidemics were first recognized and described in mule deer and elk. However, a small captive white-tailed deer herd was established at the Colorado Division of Wildlife's (CDOW) Foothills Wildlife Research Facility (FWRF; Fort Collins, Colorado, USA; 40°35'N, 105°10'W) in 1993 for use in fertility control studies. The subsequent natural occurrence of CWD in this herd afforded the opportunity to observe epidemic dynamics in captive white-tailed deer and compare them with those of contemporary cohorts of captive mule deer, which were also naturally infected with CWD.

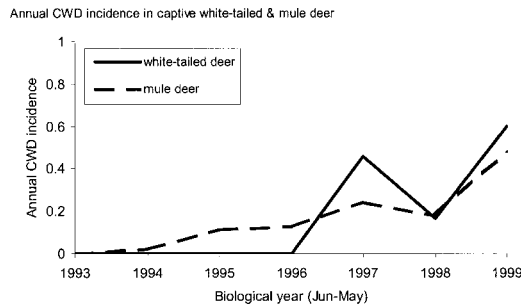


FIGURE 1. Annual incidence of chronic wasting disease (CWD) in captive white-tailed and mule deer held at the Colorado Division of Wildlife's Foothills Wildlife Research Facility (FWRF), 1993–99. Mule deer data are from Miller and Williams (2003).

Captive mule deer held in what is now the FWRF had been infected with CWD since at least the late 1960s (Williams and Young, 1992). After attempting to eradicate CWD from the FWRF in 1985 by killing all captive mule deer and elk and cleaning the facility (Williams and Young, 1992; Miller et al., 1998), a new mule deer research herd was started in 1990 with nine animals (Miller and Williams, 2003). This founder herd was augmented by natural births and “orphan” fawns. Founders and orphans were accepted only from outside areas where CWD was known to be endemic. Despite extensive preventive measures, a case of CWD was diagnosed in 1994 in a FWRF-born female from the 1991 cohort. This represented the beginning of another CWD epidemic in captive mule deer (Fig. 1), 8.5 yr after the last infected deer had lived at FWRF.

White-tailed deer had not been held at the FWRF site before 1993. In May–June 1993, 12 newborn white-tailed deer fawns were captured by hand from the Rocky Mountain Arsenal National Wildlife Refuge, a fenced enclosure where surveys conducted since 1993 have revealed no evidence of CWD in resident deer populations (Creekmore et al., 1999; Miller et al., 2000; Miller and Williams, 2003; M. W. Miller, unpubl.). After capture, fawns were transported to FWRF. There, they were held in dedicated rearing pens on the fa-

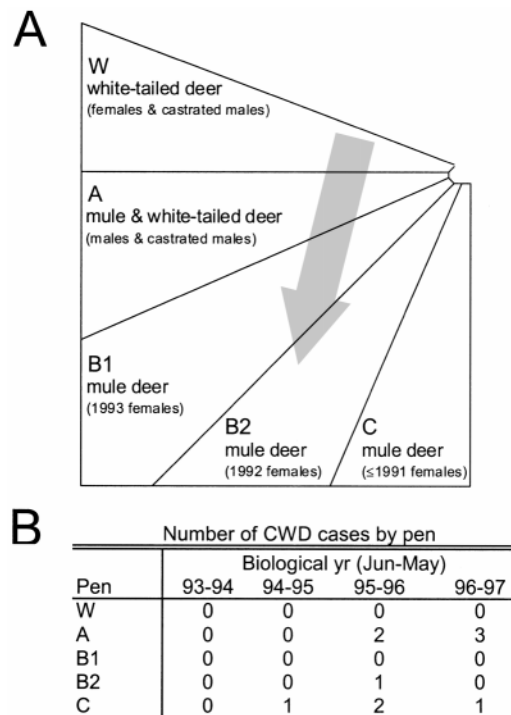


FIGURE 2. Arrangement of paddocks holding white-tailed and mule deer held at the Colorado Division of Wildlife's Foothills Wildlife Research Facility (FWRF). A. West side layout for deer paddocks and species assignments during 1993–96; gray arrow, prevailing direction of drainage and wind. B. Cases of chronic wasting disease (CWD) that occurred in deer residing in respective paddocks diagrammed in panel A. Paddock C held a group of adult female mule deer that included the index case for the ongoing CWD epidemic. After October 1996, mule deer were rearranged periodically, to accommodate research needs.

cility's east side, away from adult cervids. Fawns were fed canned evaporated milk, a pelleted feed, and alfalfa hay, using well-established rearing protocols (Wild and Miller, 1991). Eleven of 12 fawns (six females, two males, and three castrated males) survived until weaning, at which time they were moved to a new paddock (W) on the facility's west side (Fig. 2A). This new paddock, which had an electrified perimeter fence, was in proximity to other new deer paddocks and to older paddocks but had not previously held deer or elk. Weaned deer were maintained on pelleted feed, alfalfa hay, and natural veg-

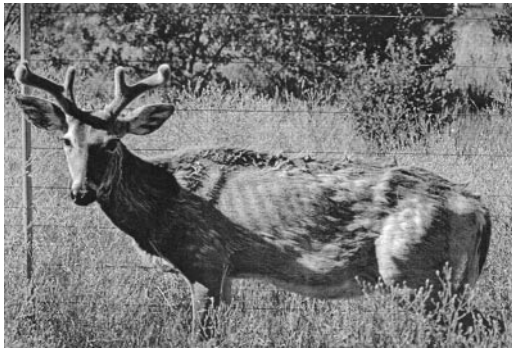


FIGURE 3. A 49-mo-old male white-tailed deer showing signs of end-stage chronic wasting disease (CWD), including emaciation, pronounced behavioral changes, ataxia, and ptalism. Signs in this animal were first noticed in May 1997, and CWD had progressed to its end stage by early July, when this photo was taken. (Photo by M. W. Miller.)

etation consisting of forbs and grasses; their diet was free from animal-derived protein. Once they were sexually mature (>12 mo old), the two males were moved into an adjacent paddock (A) during November–February each year, to prevent breeding with females; this adjacent paddock housed intact and castrated male mule deer year round. Aside from occasional research-related movements to handling and weighing facilities and isolation pens, female and castrated male white-tailed deer resided in their primary paddock throughout their respective lives.

Clinical signs suggestive of CWD (weight loss, inattentiveness, and mild depression) were first recorded in one male and one castrated male white-tailed deer in May 1997. By late June, both deer were showing signs of end-stage CWD (emaciation, pronounced behavioral changes, ataxia, and ptalism; Fig. 3), and both were killed on 8 July. The other male began showing clinical signs in late June; his condition deteriorated rapidly, and he was killed on 23 July after exhibiting an acute onset of neurological signs, including opisthotonos. A fourth deer, a female, was found dead on 27 July after several days of heavy rain and flooding at the FWRP; CWD was diagnosed postmortem. In ret-

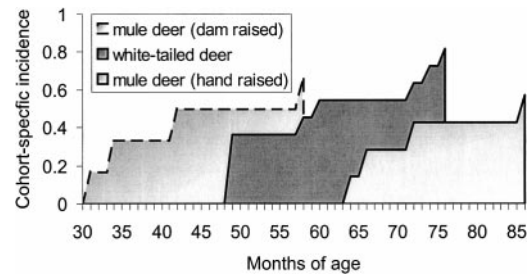


FIGURE 4. Cumulative incidences of chronic wasting disease (CWD) in 1993 cohorts of hand-raised white-tailed deer, hand-raised mule deer (HR), and dam-raised mule deer (DR). Epidemic curves, overall incidence, and range of ages at CWD-caused deaths were similar, but onsets and mean ages at CWD-caused deaths were different, among these three cohorts. Delayed onset in the white-tailed deer and HR mule deer cohorts most likely reflects delayed exposure to CWD-infected animals or contaminated environments. (See Table 1 for descriptive statistics.)

spect, early signs of CWD (particularly social isolation) had been present in this fourth animal for ~ 1 mo. Four additional deer were killed during end-stage CWD 9, 11, 23, and 26 mo after the index cases (Fig. 4). By October 1999, because only three white-tailed deer remained in the herd, and one was showing signs of CWD, the surviving deer were killed.

Chronic wasting disease was confirmed in all nine clinical cases via histopathology and immunohistochemistry (IHC), using methods described elsewhere (Williams and Young, 1993; Spraker et al., 1997; Miller et al., 2000). Accumulations of CWD-specific protease-resistant prion protein (PrP^{CWD}) were detected in multiple sections of brain (particularly the medulla oblongata, sectioned at the obex), in tonsil, retropharyngeal lymph node, and mesenteric lymph node tissues, and in Peyer's patches. Histological lesions of spongiform encephalopathy described by pathologists who evaluated these cases were indistinguishable from those described in free-ranging white-tailed deer (Spraker et al., 1997; Williams and Miller, 2002); plaques composed of PrP^{CWD} were relatively consistent among these cases

TABLE 1. Descriptive statistics for 1993 cohorts of white-tailed and mule deer naturally infected with chronic wasting disease (CWD) at the Colorado Division of Wildlife's Foothills Wildlife Research Facility, Fort Collins, Colorado. Because of likely differences in exposure histories, mule deer were divided into hand-raised (HR) and dam-raised (DR) cohorts; see text for husbandry and related details.

Species (cohort)	CWD (cases/total)	Incidence (%)	Age at CWD death (mo)	
			$\bar{x}$ (SE)	Range
White-tailed deer	9/11	82	59.6 (3.9)	49–76
Mule deer (HR)	4/7	57	72 (5)	64–86
Mule deer (DR)	4/6	67	41.3 (6.1)	31–58

(Williams and Miller, 2002). In addition to confirming infection in the nine clinical cases, postmortem examination revealed mild spongiform encephalopathy and IHC staining of brain and lymphoid tissues in one of the two apparently healthy deer killed when the herd was terminated; the other deer showed neither IHC staining nor spongiform encephalopathy postmortem.

The overall incidence of clinical CWD in this captive white-tailed deer cohort was ~82% among individuals that survived >15 mo (minimum observed incubation; Williams and Miller, 2002) (Table 1), although at least one additional case likely would have occurred if the herd had not been terminated. Affected white-tailed deer died or were killed during terminal stages of CWD at age 49–76 mo. The ages at deaths attributed to naturally acquired CWD were about threefold greater than the 16- to ≥ 30 -mo intervals from exposure to CWD-caused death observed in white-tailed deer inoculated orally with conspecific infectious brain tissue homogenate (M. W. Miller and E. S. Williams, unpubl.). This difference could reflect either delayed exposure or lower exposure doses in the naturally infected white-tailed deer. On the basis of observations of CWD epidemiology in mule deer (Williams and Young, 1992; Miller and Williams, 2003), intraspecific horizontal transmission probably sustained this epidemic; the observed patterns of cumulative incidence (Fig. 4) resembled those previously described in mule deer. The original source of exposure for these white-tailed deer could not be

determined: two of the first four cases were in male white-tailed deer that had been housed seasonally with male and castrated male mule deer in a paddock (A) where five cases of CWD in mule deer occurred during 1995–97 (Fig. 2B), but the female and castrated male white-tailed deer that died from CWD at the same time as the two males were not housed with mule deer.

Mule deer also were recruited into the FWRF herd in 1993. Thirteen fawns were added in June through births or orphan acquisitions. Seven females, including four born to FWRF dams, were hand raised (HR) until weaning using the same protocols and dedicated facilities described for white-tailed deer; six males born at the FWRF were raised by their dams (DR) in a paddock where adult female mule deer were housed. Five other hand-raised fawns (three females and two males) from outside sources (OR) were added in November. At weaning, female fawns were housed in a paddock (B1) on the west side, separate from other groups of mule deer and from the white-tailed deer (Fig. 2A); they remained in this grouping until October 1996, when deer were rearranged to accommodate research needs. By fall 1994, males and castrated males from the 1993 cohort were housed with other adult male and castrated male mule deer, apart from females. Because these fawn groups potentially had different opportunities for CWD exposure, they were regarded as separate cohorts for the purposes of comparison, designated as HR, DR, and OR to denote their divergent histories. The

early exposure history of the HR cohort most closely resembled that of the white-tailed deer cohort described earlier, although extensive rearranging of FWRF mule deer after October 1996 diminished these similarities.

General patterns of CWD occurrence in the 1993 mule deer cohorts resembled patterns seen in the 1993 white-tailed deer cohort (Fig. 4). About 57% of the HR cohort and 67% of the DR cohort developed CWD. The occurrence of CWD in the HR mule deer cohort was somewhat later than that seen in white-tailed deer (Table 1). Although cases among HR animals tended to occur later than in white-tailed deer, the range of ages at death (22 mo) was somewhat narrower than that seen in white-tailed deer. Of the three HR mule deer that did not contract CWD, two died at age ≤ 29 mo, and the third survived to age 74 mo.

Although the incidence of CWD in the DR mule deer cohort was comparable to that in both the HR and white-tailed deer cohorts, some temporal aspects of CWD epidemiology differed substantially for DR mule deer (Table 1 and Fig. 4). Clinical disease appeared to occur earlier in DR cohort mule deer than in either the white-tailed deer or HR mule deer cohorts. However, the range of ages at death (27 mo) was equivalent to the range in white-tailed deer and was wider than that in HR mule deer. Two DR mule deer that did not contract CWD died at age ≤ 37 mo.

Only two (40%) of five OR cohort mule deer, one male and one female, contracted CWD. Both of these cases fell within the range of the established mule deer cohorts that they joined: the male died 52 mo after entering the FWRF herd, and the female died 64 mo after entering. All three OR mule deer that did not contract CWD died ≤ 30 mo after arriving at FWRF.

The ages at death attributed to naturally acquired CWD were about threefold greater among HR animals and about twofold greater among DR animals than the 20- to ≥ 25 -mo ($\bar{x}=23$ mo) intervals from

exposure to CWD-caused death in mule deer that were inoculated orally with infectious brain tissue homogenate (Williams and Miller, 2002). Moreover, the range of age at death in these naturally acquired cases was at least threefold greater than that observed in experimental infections. As in the white-tailed deer epidemic, these differences could reflect either delayed exposure or lower exposure doses in the naturally infected mule deer. However, horizontal transmission most likely drove observed epidemic dynamics.

Apparent differences in mean age at CWD-caused death between the DR and HR cohorts may reflect differences in the timing or intensity of exposure to CWD. Maternal transmission appears to be far less important than horizontal transmission in contributing to risk of CWD infection in mule deer (Miller and Williams, 2003); thus, differences between these cohorts probably should not be taken as evidence of dam-offspring transmission. Although maternal transmission per se was unlikely, exposure to CWD still could have occurred earlier in DR mule deer than in the HR mule deer and white-tailed deer cohorts. In 1993, adult (≥ 2 yr old) female mule deer at FWRF were housed together in the paddock where the index case for the current epidemic occurred in 1994 (Fig. 2A). The DR fawns remained with their dams in this paddock until some time during the winter or spring, when they were moved into a paddock with older male mule deer. Of the five secondary CWD cases in the early years of the mule deer epidemic, at least four (including two DR siblings) were housed for ≥ 6 mo in the same paddock with the index case. In contrast, HR fawns were removed to the dedicated rearing facility 24–48 hr after birth; after weaning, they remained in a separate paddock until October 1996, when female groups were mixed for planned research experiments unrelated to CWD studies. It follows that the earliest exposures of HR deer to likely sources of infection (infected deer or contaminated

paddocks) may have occurred ≥ 40 mo later than exposure of DR deer (Fig. 2B). These observations are similar to findings from a study of scrapie transmission in sheep, wherein incidence was lower and average age at scrapie death higher among sheep removed from an infected flock at birth than in those removed at later ages (Hourrigan et al., 1979).

Despite the likelihood of later initial exposure in HR deer, their exposures may have been greater, either by virtue of contact with more infected animals or with larger accumulations of CWD agent in contaminated paddocks, thereby reducing the average disease course (Foster and Dickinson, 1989; Hoinville, 1996; Woolhouse et al., 1998; Miller and Williams, 2003). This may explain why the range of ages at CWD death was somewhat narrower for HR (22 mo) than for DR (27 mo) animals, even though the average age of onset was later in HR deer. The dramatic decline in ages at CWD-related death among FWRF mule deer cohorts over an 8-yr period (1991–99; Miller and Williams, 2003) is consistent with an increasing intensity of exposure over the course of this epidemic. However, observations of a higher CWD prevalence in male mule deer than in sympatric females (M. W. Miller, unpubl.) also could reflect sexual differences in exposure or susceptibility between the all-female HR and all-male DR cohorts.

On the basis of the foregoing observations, the epidemic dynamics of CWD in captive white-tailed deer were strikingly similar to those in captive mule deer held under similar conditions (Figs. 1, 4). However, timing and magnitudes of exposure, and possibly other factors, like demographic differences (M. W. Miller and M. M. Conner, unpubl.), social behavior (Conner and Miller, 2004), or prion gene polymorphisms (Brayton et al., 2004; O'Rourke et al., 2004; J. E. Jewell, pers. comm.), could influence dynamics of individual epidemics. Given the similarities in the clinical and postmortem features of

CWD in these two closely related species, similarities in epidemiology are not surprising. It follows that epidemic dynamics in sympatric, free-ranging white-tailed and mule deer that share habitats in western North American ranges also may be similar. Whether epidemic dynamics remain similar when free-ranging populations of deer reside in entirely different natural habitats seems less certain.

The transmissibility of CWD appears to differ somewhat among its three natural host species. Both annual and cohort-specific CWD incidences in captive white-tailed deer, and in mule deer observed here and elsewhere (Williams and Young, 1992; Miller and Williams, 2003), were substantially higher than rates reported for CWD in captive elk (Miller et al., 1998) also held at FWRF under similar conditions. Host factors may explain such differences. The accumulation of disease-specific PrP^{CWD} in gut-associated lymphoid tissues (GALT) (e.g., tonsils, Peyer's patches, and mesenteric lymph nodes) of a host species appears to be strongly related to the horizontal transmissibility of prion diseases (Miller and Williams, 2003). In CWD-infected white-tailed and mule deer, PrP^{CWD} accumulates early and abundantly in GALT (Sigurdson et al., 1999; Spraker et al., 2002; Williams and Miller, 2002; M. W. Miller and E. S. Williams, unpubl.), and CWD appears to be quite contagious in both species. In contrast, PrP^{CWD} accumulates later and less abundantly in GALT of elk infected with CWD (Balachandran et al., 2002; Williams and Miller, 2002), and transmissibility appears to be comparatively diminished. This relationship between contagiousness and PrP accumulation in GALT also holds for scrapie in sheep (PrP in GALT and contagious) (Hoinville, 1996; Andréoletti et al., 2000; Redman et al., 2002) and bovine spongiform encephalopathy in cattle (little or no PrP in GALT and not contagious) (Hoinville et al., 1995; Ferguson et al., 1997; Wells et al., 1998). Further study of such patterns may be helpful in predicting

the relative contagiousness of CWD and other prion diseases in natural and unnatural hosts.

We thank E. Williams, T. Spraker, and C. Sigurdson for postmortem evaluations of CWD cases; T. Davis for clinical observations, record keeping, and overall FWRF management; and A. Case and many others for hand-raising and caring for research animals at FWRF. T. Apa, D. Baker, and the Assistant Editor provided helpful comments on earlier manuscript drafts. The United States Department of Agriculture, Wildlife Services, provided initial financial support for maintaining the white-tailed deer herd. This work was funded by the Colorado Division of Wildlife and Federal Aid in Wildlife Restoration Project W-153-R.

LITERATURE CITED

- ANDRÉOLETTI, O., P. BERTHON, D. MARC, P. SARADIN, J. GROSCLAUDE, L. VAN KEULEN, F. SCHELCHER, J.-M. ELSSEN, AND F. LANTIER. 2000. Early accumulation of PrP^{Sc} in gut-associated lymphoid and nervous tissue of susceptible sheep from a Romanov flock with natural scrapie. *Journal of General Virology* 81: 3115–3126.
- BALACHANDRAN, A., T. R. SPRAKER, K. I. O'ROURKE, E. S. WILLIAMS, AND J. McLANE. 2002. Sub-clinical chronic wasting disease (CWD) in farmed Rocky Mountain elk in Canada: Histopathological, immunohistochemical (IHC) and PrP genotyping findings in the "source" farm. International Conference on Transmissible Spongiform Encephalopathies, Edinburgh, UK [Abstract P1.18].
- BRAYTON, K. A., K. I. O'ROURKE, A. K. LYDA, M. W. MILLER, AND D. P. KNOWLES. 2004. A processed pseudogene contributes to apparent mule deer prion gene heterogeneity. *Gene* 326: 167–173.
- CONNER, M. M., AND M. W. MILLER. 2004. Movement patterns and spatial epidemiology of a prion disease in mule deer population units. *Ecological Applications* 14: In press.
- CREEKMORE, T. E., D. G. WHITTAKER, R. R. ROY, J. C. FRANSON, AND D. L. BAKER. 1999. Health status and relative exposure of mule deer and white-tailed deer to soil contaminants at the Rocky Mountain Arsenal. *Environmental Toxicology and Chemistry* 18: 272–278.
- FERGUSON, N. M., C. A. DONNELLY, M. E. J. WOOLHOUSE, AND R. M. ANDERSON. 1997. The epidemiology of BSE in cattle herds in Great Britain. II. Model construction and analysis of transmission dynamics. *Philosophical Transactions of the Royal Society of London B* 352: 803–838.
- FOSTER, J. D., AND A. G. DICKINSON. 1989. Age at death from natural scrapie in a flock of Suffolk sheep. *The Veterinary Record* 125: 415–417.
- HOINVILLE, L. J. 1996. A review of the epidemiology of scrapie in sheep. *Revue Scientifique et Technique, Office International des Epizooties* 15: 827–852.
- , J. W. WILESMITH, AND M. S. RICHARDS. 1995. An investigation of risk factors for cases of bovine spongiform encephalopathy born after the introduction of the "feed ban." *The Veterinary Record* 136: 312–318.
- HOURRIGAN, J., A. KLINGSPORN, W. W. CLARK, AND M. DE CAMP. 1979. Epidemiology of scrapie in the United States. In *Slow transmissible diseases of the nervous system*, Vol. 1. S. B. Prusiner and W. J. Hadlow (eds.). Academic Press, Inc., New York, New York, pp. 331–356.
- JOLY, D. O., C. A. RIBIC, J. A. LANGENBERG, K. BEHLER, C. A. BATHA, B. J. DHUEY, R. E. ROLLEY, G. BARTELT, T. R. VAN DEELEN, AND M. D. SAMUEL. 2003. Chronic wasting disease in free-ranging Wisconsin white-tailed deer. *Emerging Infectious Diseases* 9, <http://www.cdc.gov/ncidod/EID/vol9no5/02-0721.htm>. Accessed 25 May 2003.
- MILLER, M. W. AND E. S. WILLIAMS. 2003. Horizontal prion transmission in mule deer. *Nature* 425: 35–36.
- , M. A. WILD, AND E. S. WILLIAMS. 1998. Epidemiology of chronic wasting disease in Rocky Mountain elk. *Journal of Wildlife Diseases* 34: 532–538.
- , E. S. WILLIAMS, C. W. MCCARTY, T. R. SPRAKER, T. J. KREEGER, C. T. LARSEN, AND E. T. THORNE. 2000. Epizootiology of chronic wasting disease in free-ranging cervids in Colorado and Wyoming. *Journal of Wildlife Diseases* 36: 676–690.
- O'ROURKE, K. I., T. R. SPRAKER, L. K. HAMBURG, T. E. BESSER, K. A. BRAYTON, AND D. P. KNOWLES. 2004. Polymorphisms in the prion precursor functional gene but not the pseudogene are associated with susceptibility to chronic wasting disease in white-tailed deer. *Journal of General Virology* 85: 1339–1346.
- REDMAN, C. A., P. G. COEN, L. MATTHEWS, R. M. LEWIS, W. S. DINGWALL, J. D. FOSTER, M. E. CHASE-TOPPING, N. HUNTER, AND M. E. J. WOOLHOUSE. 2002. Comparative epidemiology of scrapie outbreaks in individual sheep flocks. *Epidemiology and Infection* 128: 513–521.
- SIGURDSON, C. J., E. S. WILLIAMS, M. W. MILLER, T. R. SPRAKER, K. I. O'ROURKE, AND E. A. HOOVER. 1999. Oral transmission and early lymphoid tropism of chronic wasting disease PrP^{res} in mule deer fawns (*Odocoileus hemionus*). *Journal of General Virology* 80: 2757–2764.

- SPRAKER, T. R., M. W. MILLER, E. S. WILLIAMS, D. M. GETZY, W. J. ADRIAN, G. G. SCHOONVELD, R. A. SPOWART, K. I. O'ROURKE, J. M. MILLER, AND P. A. MERZ. 1997. Spongiform encephalopathy in free-ranging mule deer (*Odocoileus hemionus*), white-tailed deer (*Odocoileus virginianus*), and Rocky Mountain elk (*Cervus elaphus nelsoni*) in northcentral Colorado. *Journal of Wildlife Diseases* 33: 1–6.
- , R. R. ZINK, B. A. CUMMINGS, M. A. WILD, M. W. MILLER, AND K. I. O'ROURKE. 2002. Comparison of histological lesions and immunohistochemical staining of proteinase-resistant prion protein in a naturally-occurring spongiform encephalopathy of free-ranging mule deer (*Odocoileus hemionus*) with those of chronic wasting disease of captive mule deer. *Veterinary Pathology* 39: 110–119.
- WELLS, G. A. H., S. A. C. HAWKINS, R. B. GREEN, A. R. AUSTIN, I. DEXTER, Y. I. SPENCER, M. J. CHAPLIN, M. J. STACK, AND M. DAWSON. 1998. Preliminary observations on the pathogenesis of experimental bovine spongiform encephalopathy (BSE): An update. *The Veterinary Record* 142: 103–106.
- WILD, M. A., AND M. W. MILLER. 1991. Bottle-raising wild ruminants in captivity. *Colorado Division of Wildlife, Outdoor Facts*, No. 114, 6 pp.
- WILLIAMS, E. S., AND M. W. MILLER. 2002. Chronic wasting disease in deer and elk in North America. *In* *Infectious diseases of wildlife: Detection, diagnosis, and management*, R. G. Bengis (ed.). *Revue Scientifique et Technique, Office International des Epizooties* 21: 305–316.
- , AND S. YOUNG. 1980. Chronic wasting disease of captive mule deer: A spongiform encephalopathy. *Journal of Wildlife Diseases* 16: 89–98.
- , AND ———. 1982. Spongiform encephalopathy of Rocky Mountain elk. *Journal of Wildlife Diseases* 18: 465–471.
- , AND ———. 1992. Spongiform encephalopathies of Cervidae. *In* *Transmissible spongiform encephalopathies of animals*, R. Bradley and D. Mathews (eds.). *Revue Scientifique et Technique, Office International des Epizooties* 11: 551–567.
- , AND ———. 1993. Neuropathology of chronic wasting disease of mule deer (*Odocoileus hemionus*) and elk (*Cervus elaphus nelsoni*). *Veterinary Pathology* 30:36–45.
- , M. W. MILLER, T. J. KREEGER, R. H. KAHN, AND E. T. THORNE. 2002. Chronic wasting disease of deer and elk: A review with recommendations for management. *Journal of Wildlife Management* 66: 551–563.
- WOOLHOUSE, M. E. J., S. M. STRINGER, L. MATTHEWS, N. HUNTER, AND R. M. ANDERSON. 1998. Epidemiology and control of scrapie within a sheep flock. *Proceedings of the Royal Society of London B* 265: 1205–1210.

Received for publication 6 July 2003.