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Chronic wasting disease of cervids☆

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ABSTRACT

Chronic wasting disease (CWD) of cervids is the only known transmissible spongiform encephalopathy (TSE) found in non-domestic, free-ranging animals. To date, it is found in wild cervids only in North America, and natural infection has been detected in only four species (*Cervus elaphus nelsoni*, *Odocoileus hemionus*, *Odocoileus virginianus* and recently *Alces alces*) although there are concerns that it could spread to other species, particularly *Rangifer tarandus*. The infectious PrP^{CWD} spreads throughout the body, particularly in lymphoid tissue, although lesions (typical of TSEs) are found only in the brain and are associated with development of clinical disease (e.g. wasting, behavioural changes). Transmission is lateral and probably oral. Infectious prions are shed in faeces, urine and saliva, and are present in various body tissues, all of which may contribute to ante- or post-mortem environmental contamination, increasing transmission. Infectious prions persist in soils. There is presently no evidence of spread to other sympatric wildlife, domestic livestock or humans. Intracerebral inoculation enables transmission to various species of ungulates, rodents, carnivores and even primates, but oral transmission to non-cervids has mainly been unsuccessful.

1. Introduction

Chronic wasting disease (CWD) is one of the group of diseases generally known as the transmissible spongiform encephalopathies (TSE) or prion diseases, and the only known prion disease of free-living non-domestic animals. As with other prion diseases, CWD is associated with a misfolded isoform (PrP^{CWD} or PrP^{res}) of a normal cellular protein (PrP^{C}), which accumulates in the CNS, with resultant neurodegenerative changes; this abnormal PrP is transmissible (Bourne, 2004).

2. Emergence, aetiology and possible origins

CWD was first detected as a clinical wasting syndrome in mule deer (*Odocoileus hemionus hemionus*) at a research facility in Fort Collins, CO, USA, in 1967; it was recognised as a spongiform encephalopathy (SE) in 1978 (Williams and Young, 1980) and was shown to be transmissible by intracerebral (IC) inoculation into ferrets and mule deer fawns (Williams et al., 1982). The first diagnosis in captive Rocky Mountain elk (*Cervus elaphus nelsoni*) occurred in 1978 (Williams and Young, 1982); it was first diagnosed in wild cervids in 1981 (Spraker et al., 1997) and in farmed cervids in Saskatchewan, Canada (Sullivan, 1996).

The origin of CWD is uncertain; the favoured theory is that it derived from scrapie (Williams, 2005); scrapie inoculation IC into elk produced typical CWD lesions (Hamir et al., 2004). It is also possible that CWD arose de novo in deer and became transmissible (Bourne, 2004; Williams et al., 2002). Alternatively, it originated in another species,

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as yet unknown (Williams, 2005). Based on strain typing by inoculation into genotypically characterised mice, the CWD agent is different from BSE agent, TME agent and tested strains of CJD agent and scrapie agent (Bruce et al., 1997, 2000; Laplanche et al., 1999).

It is not yet certain whether there is a single or multiple strains of CWD. Epidemiological data and the marked similarity of the lesions strongly suggest that the same CWD agent is responsible for the disease in captive and free-ranging deer and elk (Williams and Miller, 2002). Studies in transgenic mice expressing cervid PrP indicated the same prion strain in analysed elk and mule deer (Browning et al., 2004), while ferret-passaged isolates from two sources showed differences in clinical presentation, survival period, lesion distribution, glycoform profile and resistance to proteolysis, suggesting different strains (Perrott et al., 2012). It is difficult to draw conclusions from such experiments because interspecies transmission can alter the characteristics of TSE agents (Sigurdson, 2008).

3. Geographical distribution

CWD was first found in research facilities in Colorado and Wyoming (Williams and Young, 1992; Williams and Miller, 2002). It has been confirmed in free-living cervids in 17 states in the USA (Colorado, Wyoming, Utah, Kansas, Nebraska, New Mexico, Texas, North Dakota, South Dakota, Wisconsin, Illinois, Maryland, Missouri, New York, Minnesota, Virginia, West Virginia) and in Canada (Alberta and Saskatchewan). In farmed cervids, it has been detected in Colorado, Nebraska, Montana, South Dakota, Kansas, Oklahoma, Minnesota, Iowa, Wisconsin, Missouri, Michigan, Pennsylvania and New York, and in Canada in Alberta and Saskatchewan (APHIS, 2012; NWHC, 2012). Occurrence and prevalence of CWD varies between states and between regions within a state; even within affected regions there are clusters of affected animals (Joly et al., 2006). There have been very few cases in cervids in North American zoos, with no evidence of the disease remaining in zoos in recent years (Bourne, 2004; Dubé et al., 2006; Williams and Young, 1992). Outside North America, CWD has been detected only in farmed cervids in Korea, associated with elk imported from Canada (Kim et al., 2005; ProMED-Mail, 2011; Sohn et al., 2002).

4. Host range

The known natural hosts of chronic wasting disease are mule deer, white-tailed deer, Rocky Mountain elk and moose (*Alces alces shirasi*) (Baeten et al., 2007; Williams et al., 2002). European red deer (*Cervus elaphus elaphus*) are susceptible on oral inoculation (Balachandran et al., 2010). Natural infection has not been reported in *Rangifer tarandus* (reindeer or caribou) (Lapointe et al., 2002; Sigurdarson, 2004). Oral transmission was successful in some reindeer; it is possible that some reindeer PRNP polymorphisms are protective against CWD (Mitchell et al., 2012). In Korea, CWD has been confirmed in Sika deer (*Cervus nippon*) and in red deer × sika deer (ProMED-Mail, 2011). Fallow deer (*Dama dama*) have been infected by IC inoculation from elk or white-tailed deer, with development of SE lesions (Hamir et al., 2010), but not by exposure to infected mule deer and a CWD-contaminated environment, suggesting lower susceptibility or delayed progression in this species (Rhyan et al., 2011). In Europe, surveillance of roe deer (*Capreolus capreolus*), red deer, fallow deer, muntjac (*Muntiacus reevesi*) and reindeer has not yet detected any cases of TSE (A.M. Barlow, pers. comm., 2004; Schettler et al., 2004; Schwaiger et al., 2004; Sigurdarson, 2004).

It has been possible to infect domestic cattle, goats and sheep by IC inoculation, although not in all individuals and with several-year incubation periods in cattle and goats (Hamir et al., 2006b, 2011; Williams and Young, 1992). Cattle failed to develop SE although PrP^{res} was detected in the CNS (Hamir et al., 2011). In sheep, only two of eight became infected: one (ARQ/VRQ at codons 136, 154, and 171) developing clinical signs, SE lesions and was PrP^{res} positive at 35 months post inoculation (mpi) and one (ARQ/ARQ) SE and PrP^{res} positive but no clinical signs at 72 months pi; two ARQ/ARQ and four ARQ/ARR were negative for PrP^{res} at 36–72 mpi (Hamir et al., 2006b). Oral transmission into cattle failed (to nine years post infection) (Hamir et al., 2011).

In carnivores, initial IC inoculation of mule deer CWD material into ferrets gave an incubation period of over a year to clinical signs (Williams et al., 1982). Serial passage reduced the incubation period to as low as 5 months (Bartz et al., 1998). Inoculation into American mink (*Mustela vison*) has also been successful, but IC inoculation of Common raccoon (*Procyon lotor*) kits with CWD failed (Hamir et al., 2007). In Wisconsin, brains of 812 mammalian scavengers were tested; the IDEXX HerdChek ELISA gave positive results in 1/11 *Mustela vison*, 1/259 *Procyon lotor* and 2/202 *Didelphis virginiana* but none were confirmed by Western blotting. The rest were all negative by ELISA (Jennelle et al., 2009).

In rodents, IC inoculation into laboratory mice produced infection in only "*a very few mice*", after >500 days incubation; serial passage in mice produced clinical disease (Bruce et al., 2000). Golden (Syrian) hamsters (*Mesocricetus auratus*) were not infected by IC inoculation of material from CWD mule deer (Williams and Young, 1992; Williams et al., 1992), but were infected following passage in ferrets, indicating that the host range of CWD can be altered by passage through other species (Bartz et al., 1998).

To date there are no known cases of human prion disease attributable to CWD transmitted to humans. Epidemiological investigations have failed to show links between prion disease in hunters or young people in North America and CWD and there is no evidence of increased CJD in Colorado or Wyoming (Belay et al., 2001, 2004; CDC, 2003). In vitro, CWD-associated PrP^{res} was shown to convert human PrP^{sen} only at very low efficiency (Raymond et al., 2000). IC inoculation of CWD-infected cervid material into transgenic mice expressing human PrP failed (Kong et al., 2005; Sandberg et al., 2010). Squirrel monkeys (*Saimiri sciureus*) inoculated IC with one CWD strain became ill at 31–34 mpi and were PrP^{res} positive (Marsh et al., 2005). Further experiments produced clinical disease in 33–53 months with 7/8 isolates IC and infection of 3/15 monkeys orally. In contrast, 15 cynomolgus macaques inoculated IC and orally remained well at 70 mpi and no PrP^{res} was detected by IHC or Western blot in the