Chronic Wasting Disease of Cervids

Peter Fennessy

Introduction

Chronic wasting disease (CWD) is a transmissible spongiform encephalopathy (TSE) of cervids. CWD was first reported in captive mule deer (*Odocoileus hemionus hemionus*) and mule deer x white-tailed deer (*O. virginianus*) hybrids on a research facility in Colorado in 1967. Subsequently it has also been described in white-tailed deer and in Rocky Mountain elk (*Cervus elaphus nelsoni*) (Williams and Young, 1980, 1982).

CWD is one of a family of TSEs which in every case (except fatal familial insomnia of humans) has been experimentally transmitted to other species, generally rodents (see Goldfarb & Brown, 1995). The TSE are characterised pathologically by the accumulation of an abnormal form of the normal prion protein (Prusiner, 1996). For some reason, the normal α-helix form of the protein can assume a β-sheet conformation which renders it insoluble and protease-resistant. The function of the normal prion protein is not known but gene manipulation studies in mice point to the protein having an important role in nerve transmission (Sakaguchi *et al.*, 1996). The progress of the disease is associated with the accumulation of the abnormal form of the protein which appears to be an autocatalytic process (Prusiner, 1996). In many cases amyloid accumulation is a feature of the TSEs but it is not universal (see Goldfarb & Brown, 1995; Spraker *et al., 1997).*

The various TSEs of both animals and humans are summarised in Table 1. In many cases there is evidence of both genetic and environmental components. For example, the most well described diseases are scrapie of sheep and some of the forms of Creutzfeldt-Jakob disease of humans. In several of these diseases, there is good evidence for a variation in susceptibility according to the genotype of the animal in terms of the amino acid composition of the prion protein at particular sites (Hunter *et al.*, 1997; Goldfarb & Brown, 1997; Aguzzi & Weissmann, 1996)

Chronic wasting disease

CWD has been reported from four captive wildlife research facilities in Colorado and one in Wyoming (Williams and Young, 1992; APHIS 1996). Several cases of CWD have also been found in wild free-ranging deer and elk in the vicinity of the infected Fort Collins facility, while affected elk have also been found in the vicinity of the Wyoming facility (Williams and Young, 1992; Spraker *et al.*, 1997). Cases have also been recognised in two zoos (one in Canada and one in Wyoming); in both cases zoos had received mule deer or elk, respectively, from suspect infected facilities (Williams and Young, 1992). More

recently in early 1996 there was a second case in Canada in an elk imported as a yearling from the US in 1989 (Sullivan, 1996). CWD has only been reported in cervids; other ruminant species which have been in direct or indirect contact have not been affected. These include bighorn sheep, moufflon, pronghorn antelope, moose, blackbuck antelope, mountain goat, and domestic cattle, sheep and goats (Williams and Young, 1992). There is no evidence that CWD is a zoonosis.

The origin of CWD is not known. Thus it is not known whether it originated among free-ranging animals or in captivity although CWD is clearly infectious with good evidence for lateral transmission. A recent survey of the infected populations in Colorado suggests that the incidence is higher in white-tailed deer than elk (Spraker *et al.*, 1997). In this survey around 95% of deer examined were apparently subclinically affected.

Infectivity of TSEs

The advent of new variant CJD (nvCJD) in the UK and the increasingly good evidence that it has arisen from ingestion of BSE-infected cattle tissue has highlighted the issue of cross-species transfer of TSEs (e.g. Collinge *et al.*, 1996). While TSEs are transmissible across species barriers experimentally by intracerebral inoculation, this is clearly not a normal route of transmission. However there is good evidence for lateral transmission from sheep to goats (Chelle, 1942) and from white-tailed deer to elk (Williams and Young, 1982). In the case of BSE, cats, several species of bovids and probably humans have become infected from consuming infected food (Wells & McGill, 1992). This would appear to be an abnormal situation with the TSEs and is possibly associated with the level of exposure of these populations to infective sources and genetic susceptibility. However, despite considerable exposure among zoo cervids and domestic dogs, no cases of BSE have ever been found (Bradley, 1997).

There is a clear distinction between cross-species infectivity of a particular TSE and within-species infectivity. For example, while there is no evidence of lateral transmission of BSE, there is good evidence for lateral transmission of scrapie in sheep and CWD in deer, although the mechanism is not known. In contrast, Kuru in humans was transmitted laterally among the *Fore* people of New Guinea through the practice of ritual cannibalism. Whether this occurred in the preparation of the brain as food and/or as a result of consumption itself is not known. Apart from BSE there is no evidence that the animal TSEs are zoonoses. Transmissible mink encephalopathy is a TSE recognised in mink in several countries. While the source of any new outbreak may well have been or is feed, it can be spread by cannibalism and by infection of fighting wounds (Bradley, 1997). The common assertion that a form of CJD found in Slovakia, Israel and Chile is associated with scrapie in sheep has now been shown to be without foundation. It is in fact a genetic or familial form of the disease caused by a mutation of the prion proteins (see Goldfarb and Brown, 1995).

A feature of the TSE infectious particles is their extraordinary resistance to standard methods of disinfection/inactivation. This explains the occurrence of the iatrogenic forms of CJD associated with the use of infected medical instruments during surgical intervention. In fact there is no single method which can guarantee complete sterilisation

of high titre infectious materials although recommendations include high temperature/high pressure autoclaving, immersion/exposure to 2 Molar sodium hydroxide or 2.5% sodium hypochlorite for at least one hour (Collins and Masters, 1996).

Experimental transmission of CWD

CWD has been transmitted by intracerebral inoculation of brain from affected deer into mustelids (mink and domestic ferrets), squirrel monkeys, mule deer and goats (E.S. Williams, pers comm; Williams and Young, 1992). However, these workers have been unable to transmit the disease to hamsters. Early attempts with mice were unsuccessful (Williams and Young, 1992) but the current situation is not clear.

Table 1 The involvement of genetics (ie genetic susceptibility) and environment (ie infective source) in the transmissible spongiform encephalopathies (TSE) of animals and humans

	Species	Genetics	Environment	Ref
Animal TSE	Sheep	Π	Π	1
Scrapie				
	Goats	Π	Π	7
BSE[1]	Cattle	(Π) [2]	Π	2
BSE - derived SE				
Feline (FSE)	Cats	?	Π	3
Bovids	Nyala	?	Π	4
	Gemsbok	?	Π	4
	Eland	?	Π	4
	Arabian oryx	?	Π	4
	Greater kudu	?	Π	4
TME	Mink	?	Π	5
CWD	Deer - Odocoileus spp	?	Π	6
	Elk - Cervus elaphus ssp	?	Π	6
Human TSE		Π	?	7,8
CJD - sporadic				
- iatrogenic		Π	Π	8
- new variant		Π	Π	9
- familial		Π[3]	?	8
Fatal familial insomnia		Π[3]	?	8
Gertsman-Straussler-Scheinker		Π[3]	?	8
Kuru		?	Π	8

[1] BSE - bovine spongiform encephalopathy, TME - transmissible mink encephalopathy, CWD - chronic wasting disease, CJD - Creutzfeldt-Jakob disease

[2] Genetic susceptibility is probably important

[3] Autosomal dominant conditions associated with mutations of the normal PRNP gene that codes for the prion protein

References
1 Hunter *et al.* (1989)
2 Goldman (1996)
3 Wyatt *et al.* (1991)
4 Wells & McGill (1992)
5 Hartsough & Burger (1965)
6 Williams and Young (1992).
7 Palmer *et al.* (1991)
8 Goldfarb and Brown (1995).

Epidemiology of CWD

The annual incidence of CWD has been variable in the research facilities. However, over 12 years, 60 deer (i.e. 90% of those resident in the Fort Collins facility for more than two years) died of the disease. The age of infected deer ranged from 1.5 to 9 years with the peak incidence at 3 to 4 years of age. According to those involved in the feeding of the animals in these facilities, no animal protein (other than milk) was ever fed to the deer. The evidence would suggest that the disease was transmitted to elk from infected deer. While the mode of transmission within species is not known, the epidemiological data would support lateral transmission. Vertical transmission may also occur.

Prevention and control of CWD

Chronic wasting disease would appear to be highly infectious (>90% of deer affected in the Fort Collins facility). Eradication has been attempted unsuccessfully on two occasions. In Wyoming all deer and elk in the facility where CWD had occurred were slaughtered. One year later new animals which had had no contact with affected deer or elk were introduced. Five years later the first case of CWD occurred. In the Fort Collins case, the animals were slaughtered and the site disinfected and spelled for a year before reintroduction. Two cases occurred, the first around three years after reintroduction. However, the replacement elk had been sourced from an area which was subsequently recognised to have had several CWD cases.

Clinical signs and diagnosis of CWD

The clinical signs are fundamentally those of ill-thrift and depression. They include weight loss, emaciation, teeth grinding, excess salivation, vacant (depressed) facial expression and lowered head carriage. Hind limb ataxia is relatively uncommon, but the animals are hyperexcitable. Consequently the differential diagnosis of any nervous or ill-thrift disorder (e.g. suspect ryegrass staggers, malignant catarrhal fever - chronic form -, fading elk syndrome, polioencephalomalacia, copper deficiency, abomasal/omasal ulceration in adult deer) should include histopathology of the brain (see Spraker *et al.*, 1997). Spraker *et al.* (1997) also subjected brain tissue from ten cases of spongiform encephalopathy (SE) in deer to immunohistochemical staining; in all cases they detected a protein which was antigenically indistinguishable from PrP^{sc} (the protease resistant form of the prion protein). In contrast the immunohistochemical testing was negative in seven deer which did not have SE Using electron microscopy they observed "scrapie associated fibrils" in brain tissue

from affected animals, but did not find any such fibrils in mule deer without lesions. Thus, the tests used for scrapie testing post-mortem would appear to be useful for deer.

The New Zealand situation

New Zealand farms red deer (*Cervus elaphus ssp*) and their close relatives, wapiti or elk. Wapiti may be imported from Canada but not from the US. In 1990 Canada placed a ban on the importation of cervids from the US in reaction to sporadic outbreaks of tuberculosis among captive ungulates in the US (Sullivan, 1996). The New Zealand importation situation requires considerable care but the quarantine procedures currently in place for importations from do take the CWD situation into account.

The New Zealand Ministry of Agriculture established a targeted active surveillance for BSE, scrapie and CWD in 1990 (Pharo 1997). Pharo (1997) also reports that from 1973 until active surveillance started in 1990, Animal Health Laboratories received submissions from 745 cases of deer exhibiting signs of CNS disorder. However, at that time, samples were often inadequate and specific diagnoses were made in only 276 cases (malignant catarrhal fever - 35%, nutritional deficiencies - 30%, bacterial diseases - 13% and polioencephalomalacia - 5%). Spongiform encephalopathy was ruled out in all cases. However, from January 1990 to September 1996, laboratory veterinarians screened 1140 cases from farmed deer with a clinical history of either nervous disease or illthrift. In all cases, pathologists excluded a TSE on the basis of clinical history and/or laboratory tests. In addition nine cases, where a TSE was explicitly stated as suspect on clinical grounds, were investigated. Again, spongiform encephalopathy was ruled out. In situations where nervous tissue has been autolysed or is unsuitable for histological screening the sample is sent to Central Veterinary Laboratory in the UK for testing for the presence of scrapie-associated fibrils.

Consequently, the current practice of strict import regulations and an active surveillance programme constitute a scientifically sound response to the risk of spongiform encephalopathies or CWD in deer in New Zealand.

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