Mad deer

The North American version of prion disease

This year there was some good news for hunters in the USA. Wisconsin's Department of Natural Resources expanded the annual hunting season for white-tailed deer—usually from early November to early December—and allowed hunting in some Southern counties to start as early as late summer. For the past few months, amateur hunters and state sharpshooters have lurked in bushes and forests shooting at anything with antlers and a white tail. There is one drawback, however: hunters are not allowed to keep the venison or even a trophy pair of antlers as all cadavers must be turned over to state officials.

The aim of this state-sanctioned mass slaughter, as some critics put it, is to kill more than 25 000 white-tailed deer. It was prompted by concerns that chronic wasting disease (CWD), a transmissible spongiform encephalitis (TSE) that is affecting the deer and elk population in the USA and Canada, could become endemic in the area. This measure was not met with enthusiasm from all sides. Many residents opposed the plan, fearing for the safety of their children and livestock in what some compared to a state of war in the 389 square mile 'Eradication Zone', and did not allow hunting on their land. But the aim is not necessarily to eradicate the disease in Southern Wisconsin—a futile goal given the dense deer population of up to 100 animals per square mile. 'We don't know [if this would stop the disease] and they would agree in Wisconsin that they don't know either,' said Elizabeth S. Williams from the University

Colorado is also trying to curtail an outbreak after several elk and deer killed by hunters and officials tested positive for the prion disease. In October 2001, the US

White-tailed deer

Department of Agriculture authorised US\$2.6 million as emergency spending in order to monitor the spread of the disease and to depopulate deer farms that harbour infected animals. Also, the US government has increased its funding for research on TSEs, and plans to spend an additional US\$42 million on proposals that are currently being called from researchers worldwide. This is indeed necessary as many of the disease's characteristics—the causative agent, the mode of transmission and whether it can cross species barriers—remain shrouded in mystery. 'Chronic wasting disease is the most mysterious of all prion diseases,' commented Adriano Aguzzi, from Zürich University Hospital's Institute of Neuropathology in Switzerland.

CWD was first described in 1967 as a clinical syndrome of unknown aetiology among captive mule deer in wildlife

research facilities in Colorado, and was eventually diagnosed as a spongiform encephalitis in 1971. In 1981, CWD was found in a free-living elk, again in Colorado. Since then, the disease has also been identified among free-living and captive elk and deer in other states ranging as far east as Illinois and, most recently, as far south as New Mexico. It has also become an increasing concern for the game farm industry as affected animals have been found in farms in South Dakota, Nebraska, Oklahoma, Colorado and Montana and across the border in the Canadian province of Saskatchewan (Figure 1).

CWD is limited to three cervid species: white-tailed deer, mule deer and Rocky Mountain elk. Although no clear proof exists, most researchers agree that it is a classical prion disease, whose other family members include bovine spongiform encephalitis (BSE), scrapie and Creutzfeldt–Jacob disease (CJD). Indeed, the pathogenesis of CWD is qualitatively similar to that of these other diseases, with spongiform lesions forming in the brain of affected animals. Diagnosis relies on an immunohistochemical identification of prion proteins in the lymph nodes, and researchers are now looking into an ELISA test, developed by Bio-Rad for mandatory BSE tests in European countries. Similar to the other TSEs, CWD inevitably leads to death. After a minimum incubation period of ~16 months, which may be even shorter in the wild, infected animals display behavioural changes, such as depression, decreased food consumption, salivation with increased drooling, head tremors and a wide-based stance. Symptomatic animals show deteriorating body condition and eventually die within a year.

Although CWD is clearly infectious, the mode of transmission remains elusive. Most likely, sick animals infect others through their saliva or urine as the infectious agent is shed through the alimentary tract. This may also include interspecies transmission, as spread between both deer species and elk has been documented. What is more disturbing, however, is the possibility of indirect transmission

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of Wyoming's Department of Veterinary Sciences. Rather, it is an attempt to curtail the disease before it becomes endemic, with the additional benefit of providing scientists with a large sample size of animals to investigate the epidemiology of CWD in the area, she explained.

Wisconsin is not the only state that is concerned about CWD. Further south,

Fig. 1. Distribution of Chronic Wasting Disease in wild and/or farmed deer and elk in North America.

through the environment—since prions are extremely resistant to degradation, they may stay infectious for years. This persistence may thus render any eradication programme futile, because the lingering prions may cause new outbreaks even if all infected animals are killed. ‘Within the endemic areas, the modelling that’s being done suggests that environmental contamination plays a role. But we don’t know the specifics about that,’ Williams

The persistence of prions may render any eradication programme futile if lingering prions cause new outbreaks

said. Hunters may also contribute to the spread of the disease by butchering animals on the spot and leaving the remains of the carcass in the wild.

Others blame the growing deer and elk farming industry as the main culprit for the spread of CWD across the USA. These enterprises keep the animals in fenced areas, either for hunters to shoot the animal of their choice or to sell the venison

and velvet antlers, the latter fetching prices of up to US\$200 a kilogram for use in traditional Asian medicine. Since infected animals have been found in such farms outside the original endemic areas of Colorado and Wyoming, critics maintain that the unmonitored transportation of animals may have contributed to the perceived spread of CWD across Western USA—the Rocky Mountains, for example, have been considered a natural barrier for CWD, but early last year, Colorado’s Division of Wildlife found two infected wild mule deer west of the mountains within the confines of an elk ranch. ‘I think for the captive animals that it is, in fact, a case where [CWD] has spread,’ Williams said. ‘It clearly has moved around with commerce.’ However, she cautions that this may not be the reason for the spread among wild animals: ‘There are two different things going on. The link between the outbreaks in captive and free-living animals is not clear,’ she said. ‘Even if the disease is the same, they are quite different in epidemiology.’ What’s more, since testing for CWD intensified during the late 1990s, the perceived

spread among free-living animals might be due to detection of infection in areas that were not previously under surveillance. ‘It is not clear if the spread is due to the spread of sick animals or to the spread of detection methods,’ Aguzzi commented.

Officials and the public in the affected states are also concerned that CWD might cause an American version of the European BSE disaster if the prion is able to cross species barriers. Clearly, there is suf-

The perceived spread among wild animals might be due to increasing surveillance of the disease

ficient biological and epidemiological evidence from the European BSE outbreak that prions are able to cause TSEs in other species, most notoriously a variant form of CJD (vCJD) in young people. As of June 2001, 101 cases of vCJD had been reported in the UK, three in France and one in the Republic of Ireland, which are thought to have been caused by the consumption of BSE-infected meat. The BSE

outbreak itself was also most likely caused by animal feed contaminated with an infectious prion strain from scrapie-affected sheep. Officials in the USA are clearly concerned about such scenarios, particularly that CWD might move to humans or cattle. Disturbingly, the death of three young people between 1997 and 2000 from CJD—two hunters and the daughter of a hunter who all regularly ate venison—has raised concerns that CWD might be transmissible to humans and cause the deadly neurodegenerative disease. But an epidemiological assessment by the Centers of Disease Control (CDC) in Atlanta, GA, has found no link, describing these cases as three different types of spontaneous CJD. 'This is anecdotal. I would not overestimate their importance,' Aguzzi commented. Nevertheless, the CDC has issued guidelines for hunters, such as removing the brain and spinal cord of any prey. The World Health Organization goes even further, recommending that no part of an infected animal should be eaten.

The other main concern is the spread of the disease to cattle, although several studies have so far found no indication of oral transmission. 'It appears that cattle are not highly susceptible to CWD but we are still into the studies,' Williams said. 'But we haven't proven the negative yet.' Indeed, as many details about the causative agent and its mode of transmission remain unknown, it might be premature to alleviate such concerns. 'We don't know what are the strain characteristics of CWD,' Aguzzi said. 'If the strain is similar to BSE, one would obviously be very worried.'

In the meantime, the federal and state governments in the USA are moving to curtail the disease. Several states have issued laws regulating the transport of

North American elk

deer and elk for commercial purposes, while a federal law is nearing completion that will further regulate the deer farm industry and introduce a herd certification programme. These measures might then help to eradicate CWD among farmed animals, thinks Williams, pointing out that Europe eventually controlled the BSE outbreak. But that does not solve the

problem in wild animals. 'The situation with free-living deer may be much more difficult,' she said, 'And there is the sticky question about environmental contamination.'

These are indeed the reasons why other countries have so far failed to totally eliminate prion diseases. Just a few thousand miles further west, the Icelandic government has been fighting the battle against scrapie using probably the harshest measures imposed by any country. If an infected animal is found, the whole herd is culled, the farm is disinfected—even the gravel around the sheds is replaced—and farmers are not allowed to introduce a new flock for three years. But this is to no avail, as scrapie remains endemic in the affected areas. 'It doesn't seem to be possible to eradicate it,' said Astridur Palsdottir from the University of Iceland's Institute of Experimental Pathology in Reykjavik, Iceland. Aguzzi agrees about the futility of such eradication programmes: 'I think that this is a good flanking measure, but I just don't believe that this will work.' Icelandic biologists are now exploring other alternatives, particularly breeding scrapie-resistant sheep to overcome the problem. Such inventive approaches might eventually provide a solution, thinks Williams. As it stands now, though, the USA will have to live with CWD for a while to come.

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