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Transmissable Spongiform Encephalopathies

Creutzfeldt-Jakob disease (CJD) is a degenerative brain disorder, usually of people over 60 years of age, that is characterized by loss of coordination and dementia. The disease, though rare (1 per 1,000,000 population), is usually fatal and has no known treatment. Most CJD cases occur sporadically with no known route of acquisition. Ten to 15%of cases are inherited in an autosomal dominant fashion. There is documentation of rare instances of CJD transmission via exposure to contaminated surgical instruments, dura mater grafts, and human pituitary-derived growth hormone.

CJD belongs to a group of animal and human diseases known as transmissible spongiform encephalopathies (TSEs). TSEs usually cause brain tissue to be riddled with holes, hence the term "spongiform." Other TSEs include: kuru, Gerstmann-Straussler-Scheinker disease, and fatal familial insomnia in humans; bovine spongiform encephalopathy; transmissible mink encephalopathy; chronic wasting disease of mule deer and elk; feline spongiform encephalopathy; and scrapie in sheep.

The agents that cause TSEs are infectious proteins called prions. Normal forms of prion protein, called PrP^{c} (**Pr**ion **P**rotein **c**ommon), are found in brain neurons. The infectious prions, called PrP^{sc} (**Pr**ion **P**rotein **sc**rapie), appear to propagate by changing the structure of normal PrP^{c} to infectious PrP^{sc} through a replication cascade.[1]

Recently, 10 unusual cases of CJD with onsets from early 1994 through late 1995 were reported in Britain. The age distribution and clinical presentation of these cases suggests that they represent a new variant of CJD (v-CJD). In contrast to classic, sporadic CJD (which typically arises in patients late in life), the 8 patients with v-CJD who died were aged 18 to 41 years and the 2 living v-CJD patients are 18 and 31. None of the 10 had a hereditary predisposition to CJD. Sporadic CJD progresses to death an average of 4 months after onset of symptoms. For the 8 v-CJD patients who died, however, intervals between disease onset and death averaged 12 months.[2]

Abnormal electroencephalogram (EEG) readings of generalized slow-wave activity progressing to paroxysmal sharp-wave activity against the slow background are a hallmark of classic CJD.[3] None of the 10 patients had characteristic EEGs. Further, these patients' brain tissue showed pathology not normally associated with classic CJD. Although on postmortem exam all 8 patients had the PrP^{sc} plaques considered diagnostic for CJD, all brain biopsies also contained unusual PrP^{sc} plaques with dense eosinophilic centers and surrounding zones of spongiform change.[2] These types of plaques have been documented in kuru[4] and scrapie, but never in CJD.

Researchers reporting the British v-CJD cases have suggested that they may be associated with ingestion of products from cows suffering from bovine spongiform encephalopathy (BSE) or "mad cow disease."[2] There was a marked increase in confirmed BSE cases in Britain from 1986 (17 cases) through 1992 (nearly 37,000 cases). This increase is believed to be a result of using animal (particularly sheep and cow) proteins in cattle feed. This practice was banned in Britain in 1989, and BSE reports began to decline a few years later in 1992.[1] Because the incubation period from

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prion exposure until onset of disease can span decades for human TSEs, the 10 recent, v-CJD cases could have had contact with infected beef before the 1989 ban.[2] Oral transmission of TSEs is known to occur. For instance, kuru was spread among the Fore highlanders of New Guinea who, in the past, honored the dead by eating their brains.[4]

On March 22 the Institute of Food Science and Technology, an international organization of scientists headquartered in Britain, issued a statement addressing CJD and beef and dairy product consumption. The report stated that transmission of BSE from cows to humans has never been documented. The report also pointed out that normal bovine products, muscle meat and dairy, are incapable of carrying the infective prions that cause BSE. The agent has been detected only in the brain, spinal cord, and retinas of infected cattle. In 1989 the British government banned these tissues from the food chain.[5]

initiating a TSE. Acetylcholinesterase has enough properties in common with PrP^{c} to react with anti-PrP^{c} antibodies, and PrP^{sc} from diseased brains has a strong acetylcholinesterase activity. However, experimental attempts to modify PrP^{c} using organophosphates have failed.[6]

Current evidence strongly supports the hypothesis that v-CJD has existed in Britain all along and is now being detected through improved surveillance. The overall incidence of CJD in Britain also has increased in the 1990s. This increase has been attributed to improved case ascertainment due to publicity surrounding the BSE epidemic and the efforts of the British CJD Surveillance Unit that was formed in 1990.

It is notable that 7 of the 10 v-CJD cases failed to fulfill the clinical criteria for even "possible" CJD due to a lack of characteristic EEG features. Only 2 of the 10 patients had diagnostic brain biopsies performed prior to being referred to the CJD Surveillance Unit. Another patient's illness was diagnosed as a "probable" case, and he was referred to the CJD Surveillance Unit. It is likely that the other 7 cases would have remained undiagnosed had the patients not been referred to the CJD Surveillance Unit for brain biopsies.[2]

Table 1: CJD Mortality in Texas by Age, 1984-1994

	Year												Average Rate*
Age Group	84	85	86	87	88	89	90	91	92	93	94	Total	1984-1994
0-19	0	0	0	0	0	0	0	0	0	0	0	0	-------
20-39	0	0	1	0	0	0	0	0	0	0	0	1	-------
40-59	2	1	1	2	3	2	1	3	2	0	1	18	0.25
60-99+	8	12	9	7	9	11	0	6	6	11	13	92	5.21
All	10	13	11	9	12	13	1	9	8	11	14	111	0.76

*Rate per 1,000,000 population per year

Several other explanations for v-CJD have been suggested. Proposed and dismissed was the idea that unusual features of v-CJD are the result of the patients' young ages. The new plaque pathology has never been documented in previous cases of CJD in younger patients.[2] Another proposed explanation focuses on an increased use of organophosphate pesticides in Britain. These pesticides kill insects by irreversibly binding to acetylcholinesterase. It is hypothesized that organophosphates react with PrP^{c} causing it to refold into PrP^{sc},

The United States Department of Agriculture (USDA) has also issued a statement in response to citizen concern, saying that importation of beef or cattle from countries where BSE exists has been

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Table 2: CJD Mortality in Texas by Race, 1984-1994

	Year												Average Rate*
Race	84	85	86	87	88	89	90	91	92	93	94	Total	1984-1994
Caucasian	7	12	11	9	10	12	1	7	8	10	12	99	0.77
Black	2	0	0	0	2	0	0	0	0	0	0	4	0.23
Hispanic	1	1	0	0	0	1	0	2	0	1	2	8	0.31

*Rate per 1,000,000 population per year

banned since 1989. The USDA's Animal and Plant Health Inspection Service (APHIS) monitors US cattle for BSE. In 10 years of monitoring, over 2,660 specimens from 43 states have been tested. No BSE has been demonstrated in any of these specimens.[7] Prior to the 1989 importation ban, 499 British cattle were known to have been imported into the US. APHIS has found and tested 464 of these cattle and none had BSE.[8] Cattle with neurologic symptoms also are routinely tested for BSE in the US. Since 1991 the Texas Department of Health has sent 245 rabies negative bovine specimens to the USDA laboratories in Ames, Iowa; again, no BSE has been detected.

The expected mortality for sporadic and familial CJD is 1 per 1,000,000 population per year. Tables 1 and 2 describe the CJD mortality data for Texas from 1984 through 1994. Table 1 shows an average of 0.76 deaths per 1,000,000 population per year from 1984 through 1994. Table 2 shows that whites in Texas are affected by CJD at higher rates than are blacks or Hispanics. Whites died from CJD at an average annual rate of 0.77 per 1,000,000 population during 1984-1994 while average annual death rates for blacks and Hispanics were 0.23 and 0.31, respectively.[9]

Texas CJD patients fit the classic CJD case description with one exception. A 35-year-old man, born in Czechoslovakia, died in 1986, following a 3-month illness. This patient's medical records indicate that he presented with ataxia, dementia, and memory loss; EEG results were consistent with classic CJD. Although no brain histology information is available, the short duration of disease and the abnormal EEG are consistent with classic, sporadic CJD in an unusually young patient.

The World Health Organization (WHO) recently drafted recommendations for the control of BSE in cattle; these include improved surveillance, strict bans on cattle-derived proteins in cattle feed, and increased TSE research. Although no definite link has been demonstrated, the recommendations also stress the need to research the hypothesis that v-CJD cases are related to BSE exposure. Finally, WHO recommends that no part of any animal showing signs of a TSE be allowed to enter the food chain. This action, if properly implemented, should keep risk of exposure to BSE to a minimum in affected countries.[10] At present there appears to be no risk in Texas or the rest of the US.

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Erratum

The identifying numbers for the public health regions (PHRs) are missing from the Endemic Arboviral Activity chart on page 6 of DPN Vol. 56, No. 11. From top to bottom the PHRs are as follows: 1, 3, 4, 5, 6, 7, 10, 11.