Creutzfeldt-Jakob Disease in Louisiana, 1980-2006

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INTRODUCTION

Transmissible spongiform encephalopathies (TSEs) are diseases thought to be caused by mutant cellular proteins found in mammalian nerve tissues. This family of diseases is known to affect a variety of animals, including: sheep (scrapie), cattle (bovine spongiform encephalopathy), mink (transmissible mink encephalopathy), deer and elk (chronic wasting disease), and humans (Gerstmann-Straussier-Scheinker syndrome, Fatal Familial Insomnia, kuru, sporadic or familial Creutzfeldt- Jakob disease, and variant Cruetzfeldt-Jakob disease).

In the early 1980s, Stanley Prusiner proved that these diseases could be transmitted by a protein (prion protein or PrP) isolated from nervous tissue of infected animals. No nucleic acid was found to be associated with infectivity, ruling out bacteria, viruses, and fungi as the causative agent of disease. Prusiner won a Nobel Prize in 1997 for his discovery of a new class of disease-causing agents.

Also in the 1980s, an epidemic of bovine spongiform encephalopathy (BSE) was described in Great Britain. Over 180,000 BSE cases among cattle have been identified since its discovery in 1986. Current thinking suggests that BSE arose from a change in cattle feeding practices in Great Britain in the late 1970s and 1980s. The BSE epidemic seems to have originated in Great Britain but has been identified in cattle from over 20 countries since it began.

A new type of encephalopathy affecting humans was identified in Great Britain in 1994. This disease resembled sporadic or familial CJD (sCJD) and was named new variant CJD, or vCJD.

Symptoms of sCJD and vCJD share some commonalities. In most people, illness onset is marked by some sort of neurological abnormality. This can range from blurred vision to slight memory loss to gross hallucinations. Dementia is always present in the disease. Patients suffer memory loss, mood changes, and judgment errors. They may lose interest, become apathetic or irritable, experience sleep disorders, intellectual decline, and disorientation. They may also experience tremors, problems with coordination and gait, and loss of motor control. In some patients, the cerebellar and visual abnormalities predominate. At the end of the disease, patients are mute, stuporous, spastic, and rigid. The disease rapidly progresses with death occurring in six months with sCJD and in 14 months for vCJD.

The incidence rate of sCJD varies by geography, but ranges from 0.3 to 1 case per million people per year, with an US average of about 0.9 cases per million people per year. Most cases of sCJD are thought to arise from a spontaneous mutation in the wildtype form of PrP protein found on cell membranes. Mutations favoring sCJD development have been identified and can be inherited or arise spontaneously. Sporadic CJD can also be passed nosocomially and iatrogenically. In the past, patients have been infected through contaminated corneal transplants and through use of contaminated surgical instruments during neurosurgery. In contrast, vCJD cases are believed to result from ingestion or inoculation of BSE infected material. A total of 194 vCJD cases have been identified worldwide to date.

POPULATION AND METHODS

Surveillance for CJD is primarily based on a review of death certificate data since the disease is rapidly fatal and final diagnosis is based on autopsy findings. Death certificates are collected and maintained by the Louisiana Office of Vital Statistics Registry and the Office of Public Health (OPH). Each death certificate lists the cause of death, whether an autopsy was performed, and demographic information. Louisiana death certificates were examined from 1980 through 2006 for deaths attributed to CJD.

In 1997, the Louisiana Legislature mandated the reporting of hospital discharge data. The Louisiana Hospital Inpatient Discharge Database, or LaHIDD, serves as the state registry containing inpatient discharge data submitted to DHH/OPH from Louisiana hospitals. Yearly LaHIDD datasets contain parish, age, admit date, demographic data, diagnosis, and outcome information on all hospital admissions. These datasets were scanned for the years 1999 through 2004 for inpatients with a diagnosis of CJD. The last dataset available is from 2004.

A case definition for Creutzfeldt-Jakob disease was developed based on available surveillance resources. A person is considered to have a case of CJD if they meet the following criteria:

1. CJD listed as the cause of death on the death certificate, or
2. CJD listed as a diagnosis on a hospital admission record followed by death, as determined by the presence of a death certificate, within six months

of the hospital admission. CJD could or could not be listed as the cause of death on the death certificate.

Incidence rates were determined using population data from the 1980, 1990 and 2000 censuses released by the US Census Bureau. Post Katrina population estimates for 2005 and 2006 also came from Census Bureau data. Age adjusted annual death rates and risk ratios were calculated by sex and race for Louisiana using methodology outlined by Holman et al. (Poisson regression at 95% CI). Causes of death were examined using both LaHIDD records and death certificates using the 9th and 10th Revisions of the International Classification of Diseases (ICD9 and ICD10). Information on education levels, parish of death, and place of death was obtained from death certificates and analyzed with ANOVA at the 95% confidence interval.

RESULTS

Using death certificates, we identified 76 cases of CJD from 1980-2006 with CJD listed as the official cause of death. After examining LaHIDD data from 1999-2004, we identified 17 people with CJD related hospital admissions. Of these, four were already identified by death certificate surveillance. Six of these 17 persons did not have a death certificate on file and are assumed to still be living. Three persons did have a death certificate on file, but they died over six months after their hospital admission for CJD and did not have CJD listed as a cause of death; thus they did not meet the case definition. The four remaining persons did meet the case definition for CJD and were included in our study. Within these two data sources, a total of 80 CJD cases were identified and used for further analysis.

An average of 2.96 CJD cases per year occurred in Louisiana from 1980 through 2006 (range 0- 6). Age adjusted incidence was highest among 70 to 74 years olds (5.49 cases per million), with 25% of all cases occurring in this age group. Only 7.5% of cases in Louisiana occurred in persons under 45 years of age. The average age at death for all CJD cases was 66.7 years. Incidence is almost stable, growing by an average of one case every fifty years (Figure 1).

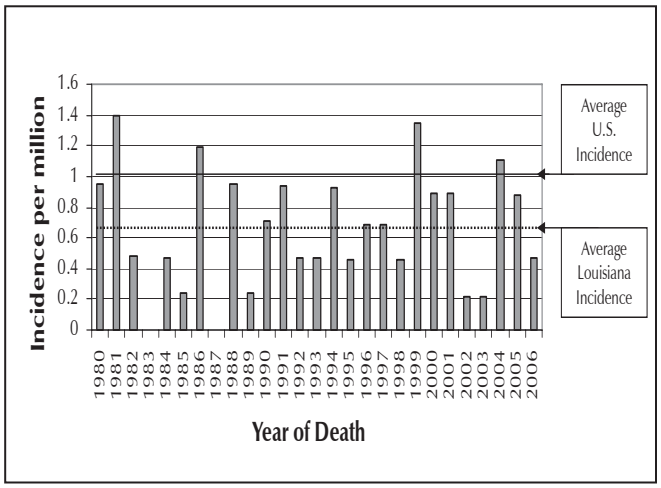

Figure 1. CJD incidence per year, Louisiana 1980- 2006.

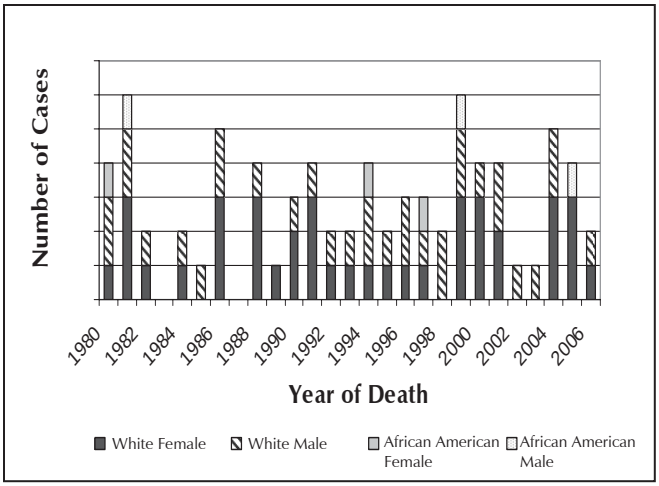

Figure 2. CJD cases by race and sex, Louisiana 1980- 2006.

Females accounted for 56% of all cases although incidence among females and males was similar (0.72 and 0.60 cases, respectively) (Figure 2). Over 91% of cases occurred among whites and whites were 5.30 times more likely to develop CJD than African Americans (OR= 5.30, 95% CI= 2.36, 12.56). Incidence peaked in females at 70 through 74 years of age while male incidence peaked later at 75 through 79 years of age. Male incidence was higher than that among females for every age over 74 years (Figure 3).

The average education level of CJD cases in Louisiana was the completion of 12th grade, or a high school diploma. Educational attainment was not a significant factor in the development of CJD when CJD cases were compared with the rest of Louisianans (F= 0.55, p=0.45). Among cases, there was wide variance in occupations, with the most often cited being 'homemaker' (26%) and 'sales' (11.7%).

Only 31% of death records recorded a place of death. Of these, 40% of cases expired during a hospital stay, 32% in nursing homes, 20% in private residences and 8% in other venues. Of the 80 CJD cases identified, only 13 (16%) had an autopsy on record.

Twenty CJD cases died between 1999 and 2004; fourteen of these had at least one hospital admission identified in LaHIDD records. The number of admissions per person ranged from 1 to 8, with an average of 2.4 admissions per person. A total of 30 admissions of CJD patients were identified. During these admissions, a total of 234 diagnoses were recorded by the admitting hospitals (each admission record contains up to eight diagnoses). Fifty-five (24%) of the diagnoses made were neurological in nature. Table 1 shows the frequency of the various neurological diagnoses. The most commonly occurring non-neurological diagnoses were related to chronic heart disease and diabetes (38% of all diagnoses).

Table 1. Neurological diagnoses of Creutzfeldt-Jakob cases from LaHIDD admission records.

Neurological Diagnoses Among CJD Cases	
Frequency	**Diagnosis**
10	Creutzfeldt-Jakob disease
11	dementia
6	convulsions
4	psychosis
3	abnormality of gait
3	lack of coordination
3	convulsive epilepsy
2	cerebral artery occlusion with complications
1	depressive disorder
1	Alzheimer's disease
1	communicating hydrocephalus
1	blurred vision
1	dizziness and giddiness
1	disturbance of skin sensation
1	aphasia
1	dysphagia
1	abnormal findings
1	diabetes with neurological manifestations
1	anxiety
1	alteration of consciousness
1	memory loss

The geographic distribution of CJD cases in Louisiana is unremarkable. Cases are clustered in high population density areas. Some smaller parishes show high incidence rates; this is due to their extremely small populations rather than a large number of cases (Figure 4).

DISCUSSION

The demographics of CJD cases identified in Louisiana mirror those of cases previously identified (Table 2).[1,2] The mean age of death, sex ratio, race ratio, and incidence rate all concur with previous studies.

No significant correlation between education level and the development of CJD was found. Occupational status was also a poor predictor of disease. Most deaths occurred among homemakers and persons in the service industry, but the age and sex of persons studied (mostly older, white females) most likely skewed the occupational distribution. A similar study in Canada yielded the same results.[3]

Very few autopsies were performed on CJD patients in Louisiana. Autopsies present a great opportunity for further study and characterization of CJD and should be encouraged. "Post-mortem examination of brain tissue specimens not only confirms a diagnosis of CJD, but also makes brain tissue available, which is crucial for furthering understanding of various subtypes of CJD, for monitoring the occurrence of CJD, and for monitoring the possibility of

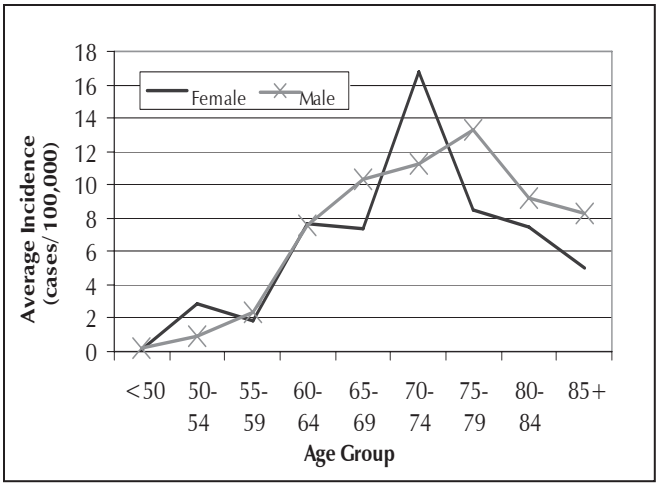

Figure 3. Average incidence of CJD by sex, Louisiana 1980-2006.

animal-to-human transmission of chronic wasting disease, a prion disease endemic in North American deer and elk populations. Barriers to autopsy (cost, family reluctance) could be surmounted by educating family members about the importance of autopsies, increasing funding for autopsies and by creating a network of pathologists qualified and willing to perform CJD autopsies."[4] The fact that 72% percent of CJD related deaths in Louisiana with place of death recorded occurred in medical or long-term care facilities is hopeful- medical staff should be encouraged to work with families to stress the importance of post-mortem examination of patients.

As of November 2006, three cases of vCJD have been identified in the United States; all of the cases consumed BSE infected meat overseas.[5,6] There have been no cases of vCJD acquired in the United States. No cases have been identified in Louisiana. Overall, surveillance indicates that annual CJD incidence in Louisiana has remained stable since 1980. There

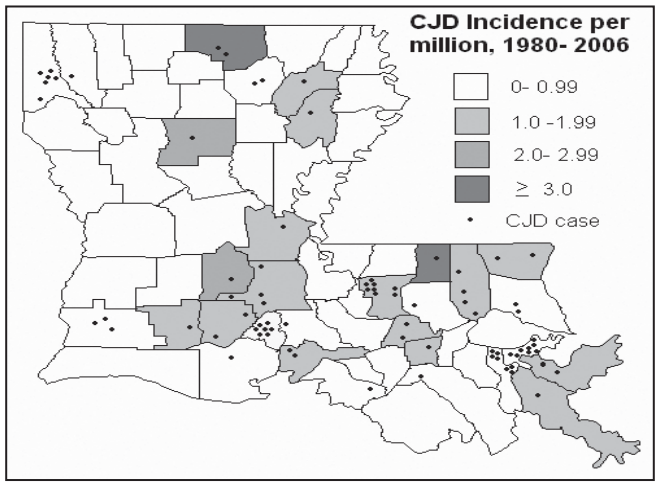

Figure 4. CJD incidence (per 1,000,000) by parish, Louisiana 1980- 2006.

Table 2. Characteristics of CJD deaths in the United States and Louisiana.

CJD Deaths and Death Rates in the United States* and Louisiana					
		United States		Louisiana	
Characteristics		**Deaths**	**Rate ****	**Deaths**	**Rate ****
Sex	Male	1714 (47%)	1.04	35 (44%)	.60
	Female	1928 (53%)	0.89	45 (56%)	0.72
Race	White	3466 (95%)	1.1	73 (91%)	0.95
	Black	125 (3.4%)	0.37	7 (9%)	0.18
	Other	51 (1.4%)	0.67	0 (0%)	0
Age Group, years					
	0-4	1	<0.01	0	0
	5-9	0	0	0	0
	10-14	0	0	0	0
	15-19	0	0	0	0
	20-24	1	<0.01	0	0
	25-29	3	<0.01	0	0
	30-34	13	0.04	1	0.12
	35-39	23	0.08	1	0.11
	40-44	39	0.16	4	0.42
	45-49	91	0.45	1	0.11
	50-54	183	0.99	4	0.54
	55-59	378	2.14	4	0.71
	60-64	598	3.55	13	2.82
	65-69	765	5.03	13	3.25
	70-74	706	5.75	20	5.49
	75-79	508	5.60	10	3.47
	80-84	225	3.94	6	3.24
	85+	108	2.42	3	1.89
Total		3642	0.95	80	.66

**Data from Holman et al.*
***Rates are per 1,000,000 population.*

has not been an increase in cases that would be indicative of vCJD transmission in Louisiana.

Surveillance through death certificates and hospital discharge data identified an average of 2.96 cases of CJD in Louisiana annually. Based on population data, we would expect to have around four cases per year. While our current surveillance system is not able to capture every case of CJD, it does identify an estimated 67% of occurring cases, with this percentage increasing each year. Because the hospital discharge and death record data already exist, they are a cost effective, reasonable method of monitoring BSE occurrence in Louisiana. This surveillance system also allows public health officials to establish a baseline incidence with which to monitor for a future possible increase due to zoonosis or other sources.

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