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disease prevention news

Creutzfeldt-Jakob Disease Update

"Mad Cow Disease" has once again become a hot media topic, which has renewed questions and concerns about the likelihood of transmission to humans and about the human disease, Creutzfeldt-Jakob Disease (CJD). The following report provides a chronology of events regarding CJD, as well as an update on current diagnostic and treatment procedures. (See also, DPN Vol.57, No. 19, September 15, 1997.)

The neurological disorder, Creutzfeldt-Jakob disease (CJD), is a transmissible spongiform encephalopathy (TSE) thought to be caused by prions, proteinaceous particles devoid of nuclei acid. [1] There is some evidence that these particles are a modified form of a normal nerve cell protein involved in synaptic function. [2] Classic CJD is the most common form; it occurs sporadically worldwide in people over age 60. It is characterized by rapidly progressive dementia accompanied by severe muscle spasms and incoordination. [3] The incidence of classic CJD is one case per million population per year. [3] Death usually occurs within 12 months of onset with an average of 8 months.[1] From 5% to 10% of patients have a less rapid course and survive more than 2 years. [4] Classic CJD has no known route of acquisition and no known treatment. Table 1 provides case definitions of the other 3 CJD types: iatrogenic, familial, and variant (v) CJD.

Historical and New Developments

CJD was first described in 1920 by H. G. Creutzfeldt and in 1921 by A. M. Jakob. Table 2 depicts a chronology of events and the discoveries of several human and animal TSEs (Table 2). Classic Creutzfeldt-Jacob disease is the most common human form (85%-90% of cases); 5-10% of cases have a hereditary predisposition (familial CJD); and less than 1% are iatrogenic, that is, result from accidental transmission.

In the 1980s scientists elucidated the nature of a new type of infectious agent subsequently called a prion. [5] Prions are widely accepted to be the etiologic agents for CJD and TSEs although there have been several other hypotheses regarding the cause of these diseases.

The Centers for Disease Control and Prevention (CDC) has been studying CJD deaths in the United States since the identification of vCJD in the United Kingdom in 1996. Variant CJD has been linked to bovine spongiform encephalopathy (BSE), also known as "mad cow disease." [6,7] Variant CJD differs from classic CJD in a number of aspects: it affects younger individuals, has a shorter clinical course, has an abnormal (but not CJD-typical) EEG, and has brain histopathology that is different but recognizable as CJD. During 1979-1994, 4,471 CJD deaths were identified in the United States; none appeared to be the vCJD type.[8]

In September 1997, the National Prion Disease Pathology Surveillance Center (NPDPSC) was established at the Division of Neuropathology of Case Western Reserve University to, among other functions, assist clinicians in the diagnosis of prion disease. (See "Diagnostic Tests" section.)

Texas Surveillance: CJD became a notifiable condition in 1998 in Texas. Because the emergence of vCJD anywhere in the US would have significant public health implications, medical records are requested and reviewed for any Texas death reported or identified through death certificate reviews as CJD. The review allows classification by type and degree of confidence in the diagnosis. The types are sporadic, familial, iatrogenic, and variant CJD; the degree of confidence is expressed as definite, probable, possible (suspect), or not a case (Table 1). Both definite and probable cases are included in reports to CDC and used to estimate incidence rates for Texas.

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Also in ths issue

Table 1. Case Definitions

Definite CJD: Neuropathologically confirmed; and/or immunocytochemically confirmed, PrP positive (Western blot) and/or scrapie associated fibrils; the findings of spongiform encephalopathy in cerebral and/or cerebellar, and/or subcortical grey matter, and/or encephalopathy with prion protein (PrP) immunoreactivity.

Probable CJD: Progressive dementia, typical periodic high-voltage complexes on electroencephalogram (EEG), and at least 2 of the following clinical features: myoclonus, visual disturbance, cerebellar disturbance, pyramidal dysfunction, extrapyramidal dysfunction, and/or akinetic mutism.

Possible CJD: Same as probable CJD but without an EEG or with an EEG finding not typical for CJD. The duration of the illness (onset of illness to time of death) is less than 2 years.

Iatrogenic CJD: Progressive cerebellar syndrome in a pituitary hormone recipient; CJD with a recognizable exposure risk, eg, dura mater transplant.

Familial CJD: Definite or probable CJD plus definite or probable CJD in a first-degree relative; neuropsychiatric disorder plus disease-specific precursor protein mutation.

Definite vCJD: Neuropathologically confirmed; and/or immunocytochemically confirmed; numerous widespread kuru-type amyloid plaques surrounded by vacuoles in both cerebellum and cerebrum; spongiform change most evident in the basal ganglia and thalamus with sparse distribution throughout the cerebral cortex. This includes neuronal loss and focal astrocytosis and high density prion protein accumulation, particularly in the cerebellum and cerebrum.

Suspect vCJD: Illness onset or death by age 55; illness duration of at least 6 months; a psychiatric presentation with anxiety, depression, social withdrawal and other behavioral changes with progression to neurological abnormalities such as progressive cerebellar syndrome, chorea, pyramidal and extrapyramidal signs; early onset of dysesthesias in limbs and face; forgetfulness and other memory impairment, dementia, and myoclonus in the late stages; an abnormal but not diagnostic EEG.

In Texas an earlier review of surveillance reports and death certificates from 1984 through 1994 revealed that all patients who had CJD had classic, sporadic disease. [9] Similarly, there have been no reports of vCJD or iatrogenic disease in Texas from January 1, 1995 through December 31, 1999. Annually in Texas, about 6 to 16 people are identified as having died from probable or definite classic CJD. The total number of confirmed cases for 1995 through 1999 was 55; 2 suspected cases for this period are still under investigation.

Clinical Course of Classic CJD

Signs of mental and or locomotor dysfunction occur early. A detailed (unpublished) review of Texas cases for 1995-1997 revealed the most common presenting symptoms to be memory impairment, cerebellar disturbance (eg, ataxia), or visual disturbance. Other motor problems included pyramidal and extrapyramidal symptoms and abnormal involuntary movement (myoclonus occurred in 73% of patients). Sensory

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problems (dysesthesias) also presented early. Paroxysmal events such as generalized and focal seizures occurred during the course of illness. In summary, the clinical course for classic CJD is variable, but common features include a long incubation period (years) and an insidious onset with sudden deterioration.[3] Some investigators categorize the observed symptom clusters as clinical types: panencephalopathic, Heidenhain's variant (presents with occipital blindness), or Brownell-Oppenheimer (cerebellar) syndrome.[1]

Diagnostic Tests

Diagnostic studies (complete blood cell count, erythrocyte sedimentation rate, electrolytes, glucose, blood urea nitrogen, calcium, phosphate, liver function, B_{12} and folate, thyroid function , serology, bacterial and viral studies, and computed tomography) are necessary to rule out treatable illnesses that should be included in the differential diagnosis for any patient with suspected CJD.[10] An encephalogram (EEG) that shows a pattern of regular or periodic high voltage, sharp wave complex bursts, superimposed on slow background activity is typical of CJD. [3] However, this pattern may not be seen until late in the course of the illness. Serial EEGs may be needed to reveal this finding.

National Institute of Neurological Disorders and Stroke (NINDS) scientists recently developed a diagnostic test to detect the presence of the 14-3-3 protein, commonly found in CJD, in the cerebrospinal fluid. When used for demented patients who meet CJD case criteria and who do not have acute stroke, this assay has a sensitivity of 95% and a specificity of 99%. With this test, it is easier to distinguish CJD from other neurological disorders, and the results are more reliable. Work is underway to develop a blood-based test for rapid detection of CJD and BSE.

NPDPSC assists clinicians in the diagnosis of prion disease by analyzing cerebrospinal fluid, blood, and brain tissue obtained either at biopsy or autopsy. Information about diagnostic services, protocols for various CJD testing, and specimen submission can be obtained at http://www.cjdsurveillance.com or by contacting the director, Dr. Pierluigi Gambetti or staff at the

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Treatment

There is still no specific treatment for CJD other than symptomatic and palliative care (to provide comfort). Pain can be relieved with opiates, and clonazepam and sodium valproate relieve muscle jerks.

Infection control measures

Although simple contact of unbroken skin with infective material is not dangerous, health care professionals who are caring for a patient with CJD should use the following precautions when handling blood and special fluid samples:

- Wear disposable gloves.
- Use universal precautions and body fluid contact isolation measures.
- Avoid self-induced injury from instruments used in the course of removing and processing tissues for pathological examination.
- Wash contaminated hands with undiluted bleach for five minutes and then thoroughly rinse the skin with water to avoid contamination of surfaces.

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Table 2. Chronology of Events

Date	Event
	Scrapie recognized in Europe for over 250 years
1920	First description of Creutzfeldt-Jakob Disease by H.G. Creutzfeldt
1921	4 other cases of CJD described by A. M. Jakob
1929	First cases of unusual occipital blindness described by Heidenhain
1936	Gerstmann-Straussler-Scheinker syndrome described
1947	Scrapie recognized in the United States in sheep
	Transmissible mink encephalopathy identified in the United States
1954	Electroencephalogram recognized as important CJD diagnostic tool
	Cases of "Heidenhain syndrome" reported by Meyer
1957	Kuru described by Carleton Gajdusek
1966	Transmission of kuru-like syndrome to chimpanzees reported by C. Gajdusek, J. Gibbs, and M. Alpers
1967	Chronic wasting disease identified in deer in the United States
1974	Iatrogenic CJD case secondary to corneal graph reported
1982	Discovery that proteinacious infectious particles cause scrapie
1985	Iatrogenic case secondary to pitituary human growth hormone reported
1986	Fatal familial insomnia described
	Bovine spongiform encephalopathy (BSE) first recognized in Britain
1987	Iatrogenic CJD secondary to dura mater graft transmission reported
1988	United Kingdom bans feeding of ruminant-derived protein to ruminants
1989	United States bans importation of live cattle, sheep, goats, and beef from Britain, and the feeding of bone meal to ruminants
1996	Cases of a variant of CJD (vCJD) described in United Kingdom
	Link between vCJD and BSE made
	Protein marker for transmissible spongiform encephalopathies found
1997	United States extends importation ban to include all of Europe
2000	USDA bans importation of protein derived products of all species from Europe
	FDA updates CJD blood donor deferral and blood donor screening recommendations

To disinfect CJD-contaminated material,

- Raise the autoclave temperature to 132-134 °C.
- Use undiluted household bleach or sodium hydroxide at 1N concentration.

Additional infection control measures for any health professionals at risk of CJD exposure (eg, pathologists or morticians who may handle tissues) is available at http://www.ninds.nih.gov/index.htm. Select "Disorders, then "CJD, and then "How Can People Avoid Spreading the disease?' OR select "publications," then "CJD, and then "CJD Fact Sheet for Health Care Workers and Morticians. The World Health Organization's year 2000 guidelines for infection control of TSEs are available at http://www.who.int/emc/diseases/bse/index.html. Another informative website is http://www.cdc.gov/ncidod/diseases/cjd/cjd.htm

Animals should not be given feed containing bone meal. In the United States importation of live cattle, sheep, goats and most ruminant products from countries where BSE was reported has been prohibited since 1989. Since 1997 this ban was widened to include importation from all of Europe. On December 7, 2000, the US Department of Agriculture prohibited all imports of rendered animal

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protein products, regardless of species, from Europe as an emergency action to prevent potentially cross-contaminated products from entering the United States.

Although there has been no evidence of transmission through blood or blood products, the World Health Organization and FDA have recommended screening of blood donors to protect blood supplies from theoretical risk of CJD transmission.

Summary

CJD became a notifiable condition in 1998 in Texas. Multiple information sources, including death certificate reviews, revealed that all cases identified for years 1984-1999 have been classic, sporadic disease. The emergence of vCJD and the worldwide concern about its transmission among humans and their domestic animals has resulted in scientists making progress in elucidating the nature of prions and TSEs. There is hope that this knowledge can help prevent the suffering these conditions cause humans and other animals.

Prepared by Olga Nuno, MD, MPH, Infectious Disease Epidemiology and Surveillance.

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Update on Meningitis Activity in Texas This Winter

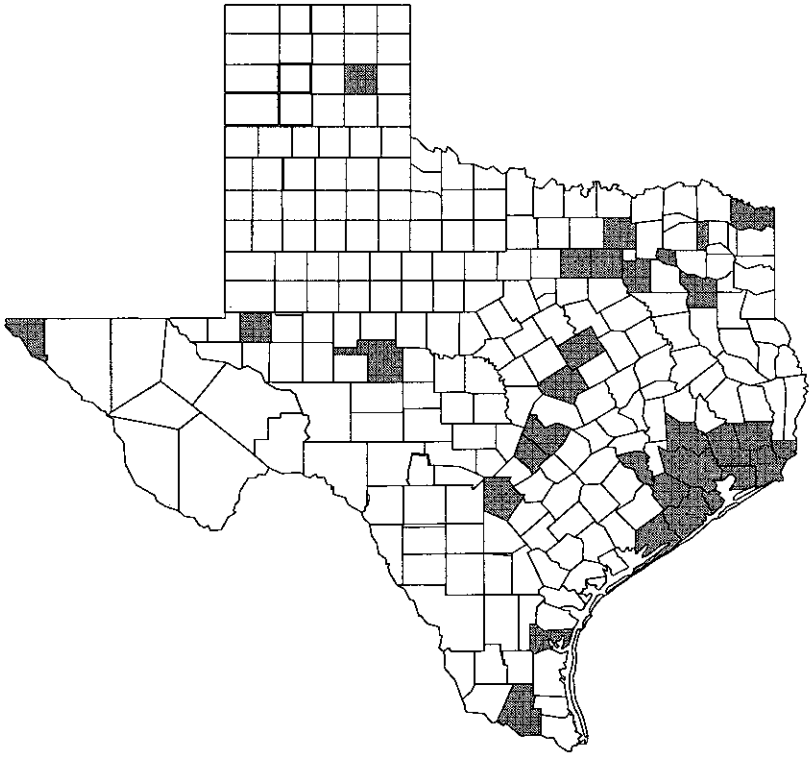
This report is an update of the one published in the February 12, 2001, *Disease Prevention News*, which described one institutional and two community outbreaks of meningococcal disease (MD) in PHR 6/5S. From November 1, 2000, through February 28, 2001, 46 laboratory-confirmed MD cases were reported from Austin, Brazoria, Chambers, Fort Bend, Galveston, Hardin, Harris, Jefferson, Liberty, Matagorda, Montgomery, and Orange Counties in PHR 6/5S. The regional case rate for this time period was 0.91 per 100,000 population. Three MD cases were reported in the two communities targeted for vaccination since the vaccination campaign (described in the above *DPN* report) ended February 1, 2001. Two school-aged children developed disease within days of receiving the vaccine; therefore, their immune response was not sufficient to prevent disease. The third patient was a 3-year-old girl who missed the vaccination effort while traveling out of state. All cases were from Montgomery County

During this same 4-month period, 36 cases had been reported from Bell, Bexar, Bowie, Collin, Dallas, Ector, El Paso, Franklin, Gray, Hays, Hidalgo, Kaufman, McLennan, Nueces, Rains, Smith, Tarrant, Tom Green, and Travis Counties. The case rate for the rest of Texas is 0.24 per 100,000 population for the 4-month period. The total number of cases reported for this period is 82. The average number of cases reported for the previous 10 years during this same period is 74. (See *DPN* Vol. 61, No. 3.) Nationally the case rate for this period is 0.34 per 100,000 population.

Isolates of *Neisseria meningitis* cultured from normally sterile sites must be sent promptly on ice to the TDH Bureau of Laboratories for confirmation and serogroup identification.

For further information contact Neil Pascoe, RN, BSN, CIC, by phone at 512/458-7676 or by email at neil.pascoe@tdh.state.tx.us.

Meningococcal Disease in Texas 11/1/2000-2/28-2001, by County



Increased Presence of Measles and Pertussis in Texas

Measles

The Texas Department of Health (TDH) Immunization Division is proud to lay claim to another measles-free year for 2000, but the news is not so good for 2001. On Friday, February 16, the Division was notified of a suspected measles case in a 10-month-old Chinese adoptee who had just arrived in Texas. In fact, this child was taken immediately from the airport to the Texas Children's Hospital in Houston where a measles diagnosis was made. The TDH Bureau of Laboratories has confirmed this diagnosis.

A second Texas child from the same adoption agency in China is currently symptomatic and that case is still under investigation as of March 2, 2001. At the time the first ill child developed her rash, approximately 9 other adoptees from 2 or 3 Chinese agencies were en route to Texas on this flight. The parents of almost all these children were contacted and immune globulin was administered within the 72-hour time frame to control the spread of measles. Outbreaks of both measles and varicella were reported in the Chinese adoption agencies from which the babies came.

Clinical Case Definition (Centers for Disease Control, September 1996)
An illness characterized by

- Generalized rash lasting ≥ 3 days, **and**
- Temperature ≥ 38.3 C (101 F), **and**
- Cough, or coryza, or conjunctivitis

Laboratory Criteria for Diagnosis

- Isolation of measles virus from a clinical specimen, **or**
- Significant rise in measles antibody level by any standard serologic assay, **or**
- Positive serologic test for measles IgM antibody

Case Classification

Suspect: any rash illness with fever
Probable: a case that meets the clinical case definition, has no or noncontributory serologic or virologic testing, and is not epidemiologically linked to a probable or confirmed case
Confirmed: a case that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a confirmed or probable case. A laboratory-confirmed case does not need to meet the clinical case definition.

Imported cases should be classified as follows:
International: a case that is imported from another country
Out of state: a case that is imported from another state in the United States. The possibility that a patient was exposed within his or her state of residence should be excluded; therefore, the patient either must have been out of state continuously for the entire period of possible exposure (at least 7-18 days before rash onset) or have had one of the following types of exposure while out of state:

- Face-to-face contact with a person who had either a probably or confirmed case, **or**
- Attendance in the same institution as a person who had a case of measles (eg, in aschool, classroom, or day care center)

Indigenous: a case if measles that is not imported. Cases that are linked to imported cases should be classified as indigenous if the exposure to the imported case occurred in the reporting state. Any case that cannot be proved to be imported should be classified as indigenous.

Note: Two probable cases that are epidemiologically linked would be considered confirmed, even in the absence of laboratory confirmation. Both probable and confirmed cases should be reported immediately to TDH by calling 800/252-9152.

For further information, including sample submission, contact Jan Pelosi at 800/252-9152; jan.pelosi@tdh.state.tx.us

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http://www.tdh.state.tx.us/phpep/

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Pertussis

Texas continues to experience high levels of pertussis morbidity. Two pertussis deaths were reported in 2000, and 2 more already in 2001. A Dallas County infant experienced onset of symptoms February 5, 2001, and died 4 days later. Five additional cases of pertussis were epidemiologically linked to this case: 2 siblings and 3 next door neighbor siblings. An infant from Midland, aged 2 ½ months, died on February 18. This case is was still under investigation as of March 2.

Clinical Case Definition (Centers for Disease Control and Prevention, September 1996
A cough illness lasting ≥ 2 weeks with one of the following:

- Paroxysms of coughing, **or**
- Inspiratory "whoop," **or**
- Post-tussive vomiting, without other apparent cause

Laboratory Criteria for Diagnosis

Isolation of *Bordetella pertussis* from clinical specimen

Case Classification

Probable: meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to a laboratory-confirmed case

Confirmed: a clinically compatible case that is laboratory confirmed or epidemiologically linked to a laboratory-confirmed case

Note: The clinical case definition above is appropriate for endemic or sporadic cases. In outbreak settings, a case may be defined as a cough illness lasting at least 2 weeks. Because some studies have documented that direct fluorescent antibody testing of nasopharyngeal secretions has low sensitivity and variable specificity, this test should not be relied on as a criterion for laboratory confirmation. Serologic testing for pertussis is available in some areas but is not standardized and, therefore, should not be relied on as a criterion for laboratory confirmation for national reporting purposes. Both probable and confirmed cases should be reported immediately to TDH by calling 800/252-9152.