



THE CITY OF NEW YORK

DEPARTMENT OF HEALTH AND MENTAL HYGIENE

Michael R. Bloomberg

Mayor

Thomas R. Frieden, M.D., M.P.H.

Commissioner

nyc.gov/health

January 23, 2006

Diagnosis and Reporting of Transmissible Spongiform Encephalopathies Including Creutzfeldt-Jakob Disease

Dear Colleague:

In July 2001, the New York City Board of Health added transmissible spongiform encephalopathies (TSEs) to the reportable disease list in the New York City Health Code (Section 11.03) due to concerns about the potential introduction or emergence of variant Creutzfeldt-Jakob disease (vCJD) in the United States. The New York City Department of Health and Mental Hygiene (NYC DOHMH) is sending this update to remind medical providers to:

- Consider TSEs** in the differential diagnosis of patients presenting with progressive dementing disorders.
- Report suspect cases** to the DOHMH so that we can assist you with obtaining diagnostic testing and investigating the mode of acquisition.

TSEs are a group of fatal degenerative diseases that affect the central nervous system and can occur in humans and certain animal species. The most common TSE affecting humans is Creutzfeldt-Jakob disease (CJD), which has a worldwide rate of approximately one case per million people each year. CJD is one of the most rapidly progressive dementing disorders in the United States. It affects several hundred people a year, typically over the age of 45, and incidence increases with age.

CJD presents with insidious progressive mental changes over a period of weeks to months, often with confusion, disorientation, speech changes, memory impairment, and subtle changes in movement, particularly noticeable in coordination or gait. As the disorder progresses, myoclonus may occur. Sometimes an exaggerated startle reflex is present, so that a loud noise will cause a whole body jerk. In some patients, vision is affected first; the patient is apparently unable to see properly because of brain dysfunction since the eyes, including optic nerve function, remain normal. In some patients, the first symptoms predominantly affect movement, with imbalance, tremor, and dyscoordination, and little accompanying cognitive change until later in the illness.

Evaluation of patients with progressive dementia should initially include general medical history and examination, neurological and psychiatric examinations, and blood testing to rule out other causes. If CJD remains in the differential diagnosis, the following specialized testing is recommended:

- Lumbar puncture (LP)** – Examination of the cerebrospinal fluid (CSF) helps exclude treatable infectious or inflammatory disorders of the central nervous system, such as herpes simplex encephalitis or other meningoencephalitides. CSF can also be analyzed for the levels of neuronal proteins known as 14-3-3 and tau, which in CJD are often markedly elevated. These tests, however, are not definitive, as not all patients have elevated levels, and because other destructive brain disorders (viral encephalitides, recent cerebral infarction or hemorrhage, hypoxic brain damage) may also result in high levels of these proteins.
- Electroencephalography (EEG)** – EEG findings in CJD may show rather periodic bursts of nearly symmetrical, but abnormally synchronized, electrical activity in the front of the brain. This pattern is not definitive, since not all CJD patients show this classic pattern, and because these EEG findings are also associated with other neurologic conditions.
- Magnetic resonance imaging (MRI)** – MRI using Diffusion-Weighted Imaging (DWI) or Fluid-Attenuated Inversion Recovery (FLAIR) sequences may show high signals that are highly suggestive of CJD. But again, such signals are not diagnostic, as about 50% of CJD patients do not have these, and other disorders can cause these abnormalities.

None of the above tests is individually either sensitive or specific enough to correctly identify all cases of CJD. However, the likelihood of CJD is high in patients presenting with a suggestive clinical syndrome and two or three of the above findings.

- Pathology examination** – Brain biopsy and autopsy are the definitive ways to diagnose TSEs, and to exclude other disorders. Some brain biopsies may be nondiagnostic because the disease process may not uniformly affect all regions of the brain. Therefore, a repeat biopsy is sometimes needed. Autopsy, which involves examination of the entire brain, is definitive.

Progression of CJD is relentless, typically with increasing disability over days and weeks and death within months; rarely does the disease course last years or decades. The disorder is caused by an increasing accumulation of an abnormal form of a nerve cell protein, the prion protein.

There are various types of CJD (See Tables 1 and 2) including:

- Sporadic CJD** – with no known cause, accounts for 85% to 90% of CJD cases.
- Familial CJD** – occurs because of a genetic mutation and accounts for about 10% of cases.
- Iatrogenic CJD** – may rarely occur due to use of contaminated neurosurgical electrodes, instruments, corneal or dura mater grafts, or due to use of cadaveric human pituitary growth hormone preparations; accounts for < 5% of cases.
- Variant CJD** – differs from CJD in its symptoms, in that vCJD often includes early psychiatric manifestations (such as anxiety, apathy, delusions, depression, and withdrawal) and abnormal sensations. MRI and EEG findings differ from classic CJD and age at onset is typically younger, with vCJD patients presenting between the ages of 15-40 years. vCJD first appeared in the United Kingdom in the 1990s, likely due to exposure to beef from cows with Bovine Spongiform Encephalopathy (BSE), a TSE affecting bovines. To date there have been two cases of vCJD in the United States, (only one of which has been confirmed) both due to exposure in the United Kingdom. There have not yet been any domestically acquired vCJD cases in the United States.

Currently there is no treatment to prevent, slow, or alter the course of CJD. The only treatments are supportive and to provide comfort to the patient and the patient's family.

There is no known person-to-person transmission. Only nervous system tissue and fluids have significant infectivity. No special precautions need to be taken with saliva, sweat, or excretions. For vCJD, there have been two confirmed cases of transmission through transfusion; thus there is a theoretical but very low risk of infectivity in blood. Standard blood precautions should be observed.

Suspected or confirmed cases of CJD or vCJD should be reported to the DOHMH. During normal business hours, contact the Bureau of Communicable Disease: Telephone: (212) 788-9830 (Main number) or (212) 442-9050 (CJD surveillance coordinator) FAX: (212) 676-2688. After hours, call the Poison Control Center at (800) 222-1222.

Please also complete the DOHMH's Universal Reporting Form using the code "TSE." Forms may be obtained by calling the Provider Access Line (PAL) (866) NYC-DOH1. Forms are also available on the DOHMH Web site at www.nyc.gov/html/doh/html/hcp/hcp-urfl.html. Please mail the completed form to: New York City Department of Health and Mental Hygiene, Bureau of Communicable Disease, 125 Worth Street, Room 214, CN6, New York, New York 10013

We strongly encourage providers to obtain autopsies on suspected CJD patients. We encourage you to discuss the importance of brain tissue for confirming the diagnosis with the patient's family at an appropriate time. In cases with suspected CJD, autopsy is usually limited to the brain only. Autopsy allows definitive diagnosis, including testing at the National Prion Disease Pathology Surveillance Center (NPDPS). The NPDPS will cover all autopsy costs, including transportation if necessary, for cases coordinated through the Center. For help with autopsy coordination the NPDPS may be contacted Monday-Friday, 8:30 AM to 5:00 PM, at (216) 368-0587. Information for evening and weekend hours is provided by voice mail at this number, and at <http://www.cjdsurveillance.com>.

Given the potential public health importance of a confirmed vCJD case in New York City, fatal cases with suspected vCJD should be reported immediately to the Office of the Chief Medical Examiner at (212) 447-2030. Autopsies will be performed on all suspected vCJD cases lacking a pre-mortem pathologic diagnosis. To ensure detection of vCJD cases in NYC, the DOHMH and the Office of the Chief Medical Examiner will work with you to ensure that an autopsy examination is performed for any suspected case of CJD or TSE aged less than 55 years.

Patients' families should be advised about supporting organizations. The CJD Foundation (www.cjdfoundation.org) operates a national toll-free Help Line (800) 659-1991 to assist families.

As always, we appreciate the ongoing collaboration of the medical and laboratory communities in helping monitor for new and emerging infectious diseases in New York City.

Sincerely,



Thomas R. Frieden, M.D., MPH
Commissioner

Free Diagnostic Laboratory Testing for Prion-Related Disease is Available at Case Western Reserve University:

The CDC, in conjunction with the American Association of Neuropathologists, has established the NPDPS at Case Western Reserve University in Cleveland, Ohio. This Center performs testing for the 14-3-3 CJD marker protein in CSF. They also perform histopathology, immunohistochemistry and Western blots on biopsy and autopsy tissues to determine the presence, distribution, and type of protease-resistant prion protein. With consent, they perform prion protein gene sequencing to determine the presence of pathogenic mutations. Tests are provided free of charge and results are reported back in a timely manner. Information on tests, specimen collection and shipping instructions can be obtained by calling the NPDSC at (216) 368-0587 or via their Web site at <http://www.cjdsurveillance.com>.

Table 1: Diagnostic Criteria for Creutzfeldt-Jakob Disease (CJD)

Sporadic CJD

Definite:

Diagnosed by standard neuropathological techniques; and/or immunocytochemically; and/or Western blot confirmed protease-resistant PrP; and/or presence of scrapie-associated fibrils.

Probable (routine investigations should not suggest an alternative diagnosis):

Progressive dementia; and at least two out of the following four clinical features:

- Myoclonus
- Visual or cerebellar signs
- Pyramidal/extrapyramidal signs
- Akinetic mutism

and

- A typical EEG during an illness of any duration and/or
- A positive 14-3-3 CSF assay and a clinical duration from onset to death of <2 years

Possible:

Progressive dementia; and at least two out of the following four clinical features:

- Myoclonus
- Visual or cerebellar signs
- Pyramidal/extrapyramidal signs
- Akinetic mutism

and

- No EEG or atypical EEG and
- Duration <2 years

Iatrogenic CJD

Progressive cerebellar syndrome in a recipient of cadaveric human pituitary growth hormone preparations; or Sporadic CJD with a recognized exposure risk, e.g., antecedent neurosurgery with dura mater implantation.

Familial CJD

Definite or probable CJD plus definite or probable CJD in a first degree relative; and/or Neuropsychiatric disorder plus disease-specific PrP gene mutation.

Table 2: Diagnostic Criteria for Variant Creutzfeldt-Jakob Disease

Definite vCJD: Neuropathologic examination of brain tissue is required to confirm a diagnosis of vCJD. The following confirmatory features should be present.

- A) Numerous widespread kuru-type amyloid plaques surrounded by vacuoles in both the cerebellum and cerebrum, resulting in a daisy-like appearance described by the term “florid plaques.”
- B) Spongiform change and extensive prion protein deposition shown by immunohistochemistry throughout the cerebellum and cerebrum.

Suspected vCJD: The following features should be present:

- A) Current age or age at death <55 years (a brain autopsy is recommended, however, for all physician-diagnosed CJD cases).
- B) Persistent painful sensory symptoms and/or psychiatric symptoms at clinical presentation.
- C) Dementia, and development, within 4 months after illness, of ataxia and at least one of the following three neurologic signs: myoclonus, chorea, or dystonia.
- D) A normal or an abnormal EEG, but not the diagnostic EEG changes often seen in classic CJD.
- E) Duration of illness of over 6 months.
- F) Routine investigations of the patient do not suggest an alternative, non-CJD diagnosis.
- G) No history of receipt of cadaveric human pituitary growth hormone preparations or a dura mater graft.
- H) No history of CJD in a first-degree relative or prion protein gene mutation in the patient.

NOTE: If a patient has the typical bilateral pulvinar high signal on MRI scan, a suspected diagnosis of vCJD requires the presence of a progressive neuropsychiatric disorder, D, E, F and G of the above criteria; and four of the following five criteria: 1) early psychiatric symptoms (anxiety, apathy, delusions, depression, withdrawal); 2) persistent painful sensory symptoms (frank pain and/or dysesthesia); 3) ataxia; 4) myoclonus or chorea or dystonia; and 5) dementia. A history of possible exposure to bovine spongiform encephalopathy (BSE) such as residence or travel to a BSE-affected country after 1980 increases the index of suspicion for a variant CJD diagnosis.

