



THE CITY OF NEW YORK

DEPARTMENT OF HEALTH AND MENTAL HYGIENE

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2004 Health Update #5: Surveillance for Transmissible Spongiform Encephalopathies, including the Classic and Variant Forms of Creutzfeldt-Jakob Disease, in New York City

Please distribute to colleagues in Neurology, Pathology, Internal Medicine, Geriatric Medicine, Infectious Diseases, Infection Control, and Family Practice

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Dear Colleagues:

In December 2003, a cow slaughtered on a farm near Yakima, Washington was confirmed to have a positive test for Bovine Spongiform Encephalopathy (BSE) or "mad cow disease". The United States Department of Agriculture (USDA) has stated that this isolated bovine case does not indicate any increased risk to the American beef supply. But given the increased attention this case has brought to prion-related diseases, such as BSE, the New York City Department of Health and Mental Hygiene (DOHMH) is sending this update to remind New York City healthcare providers that any suspected or confirmed cases of transmissible spongiform encephalopathies (TSEs) should be reported and that the DOHMH can offer assistance in obtaining diagnostic testing (including autopsies), if indicated. This update also provides information on the recent BSE-positive cattle in Canada and the United States, as well as new developments regarding TSEs, including diagnostic criteria and the availability of free laboratory testing.

On July 28, 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. TSEs, such as the classic and variant forms of CJD and kuru, are prion-mediated diseases that cause progressive neurodegenerative disorders. These diseases have long incubation periods and cause characteristic spongiform changes in the brain tissue resulting in fatal dementing illnesses.

Recent Reports of Bovine Spongiform Encephalopathy in Canada and the United States

On May 20, 2003, Canadian authorities reported a single case of BSE in a cow in Alberta, which was identified through routine surveillance. The case farm, the potential source farms, and other farms at risk were placed under quarantine. No meat from this BSE-infected cow entered the human food supply; however, meat from the cow had been used to make dog food, which officials have since recalled. More than 2800 animals in total have been depopulated and tested as part of this investigation. All test results have been negative on both Prionics Western Blot and immunohistochemistry techniques and all quarantines have been lifted.

Overall in 2003, Canada tested a total of approximately 10,000 cattle for BSE. Future testing will focus on animals that have any disease, or are found down, dying, or dead on farms. In response to this BSE case, the United States Department of Agriculture (USDA) placed a temporary import restriction on ruminants and ruminant products from Canada, pending further investigation. The United States has since partially reopened its borders to Canadian beef.

Starting in 1989, the USDA began taking steps to prevent BSE from entering the United States, including severe restrictions on the importation of live ruminants, such as cattle, sheep and goats, and certain ruminant products from countries where BSE was known to exist. The USDA tested over 20,000 cattle annually in 2002 and 2003 for BSE using a targeted surveillance approach designed to test high-risk animals for BSE. This included downer animals (animals that are non-ambulatory at slaughter), animals that die on the farm, older animals and animals exhibiting signs of neurological distress. Overall, the USDA has tested over 57,000 cattle since 1990.

The recent BSE positive cow in Washington State was the first time that an infected animal has been detected in the United States since May 1990, when active surveillance and testing began. This cow was a “downer” and was included in the (USDA’s) targeted BSE surveillance program. This diagnosis was confirmed by the BSE international reference laboratory in the United Kingdom. The US Food and Drug Administration (FDA) and inspectors from Oregon and Washington have located all potentially infectious rendered products from this BSE-positive cow. The rendering plants that processed this material have placed a voluntary hold on all known potentially infectious products, none of which had left the control of the companies or entered commercial distribution. The USDA traced the birth of the BSE-positive cow to a farm in Alberta, Canada near the farm where the Canadian BSE case was detected in May 2003.

The USDA is currently reevaluating its BSE screening program and considering, both increasing the number of cattle tested as well as looking into more rapid tests such as are currently being used in Europe. It is estimated that about 195,000 cattle are non-ambulatory or sick at slaughter and therefore eligible for testing. On December 30, 2003 the USDA announced additional safeguards to further minimize the risk of human exposure to BSE in the US. These include

- ❖ An immediate ban on the use of non-ambulatory (“downer”) cattle for human consumption.
- ❖ Any cattle tested for BSE will not be marked as “inspected and passed” until negative test results are received.
- ❖ Specified risk material (SRM) will be prohibited for use in the human food supply. These include the skull, brain, trigeminal ganglia, eyes, portions of the vertebral column, spinal cord and dorsal root ganglia of cattle over 30 months of age, and the distal ileum and tonsils in cattle of all ages.
- ❖ Use of mechanically-separated beef in the human food supply will be prohibited.
- ❖ Air-injection stunning of cattle will be prohibited, to ensure that portions of the brain are not dislodged into the tissues of the carcass as a consequence of this procedure.

CJD and variant CJD in the United States

Most CJD cases are sporadic (approximately 90% of cases), though iatrogenic transmission (<1% of cases) and autosomal dominant inheritance (approximately 10% of cases) also occur. Annual CJD deaths have remained relatively stable in the United States at approximately 1 case per million population. Variant CJD (vCJD) was first reported in 1996 in the United Kingdom, where an outbreak of BSE had occurred among cattle since the early 1980s. Transmission is believed to occur primarily through the consumption of processed food items that contain infectious bovine tissues such as the brain or spinal cord. There is strong epidemiologic and laboratory evidence for a causal association between BSE and vCJD. The absence of confirmed cases of vCJD in BSE-free geographic areas supports a causal association.

With the increasing recognition of BSE throughout Europe, there have been concerns that cases could occur among United States residents with prior exposure to contaminated meat overseas. In April 2002, the Florida Department of Health and the Centers for Disease Control and Prevention (CDC) reported a

suspect case of vCJD in a 22-year old British citizen residing in Florida. The patient's clinical condition and travel history are consistent with vCJD acquired in the United Kingdom. This individual was born and raised in Britain and lived there during the peak of the BSE epidemic in the 1980s and early 1990s before moving to the United States. This is the only reported case of vCJD in the United States.

Chronic Wasting Disease in Elk and Deer in the United States

The importance of having strong prion disease surveillance in the United States has been further underlined by recent reports that chronic wasting disease (CWD), an endemic prion disease affecting elk and deer which is found in an increasing number of states in the Midwest and Southwest, may be transmitted to humans generating a new prion disease. The World Health Organization (WHO) and the CDC agree that there currently is insufficient evidence to establish a link between human disease and handling or consuming CWD-infected deer. Although no human cases of CWD have been identified, laboratory research suggests that it is theoretically possible; however it is believed that the risk to humans is low.

Requirements for Reporting CJD and other TSEs to the New York City DOHMH:

Given the increasing public concern about vCJD and the possibility of new forms of TSEs, the DOHMH has implemented enhanced surveillance for all suspect or confirmed cases of TSE. The New York City Health Code Section 11.03 was amended as of July 28, 2001, to include reporting of any form of CJD and other TSEs as soon as these are diagnosed or suspected. We encourage providers to request laboratory testing for the 14-3-3 protein and/or brain biopsy or autopsy on suspect cases as well as to report both suspected or confirmed cases of CJD or other TSEs. When you report a suspect case to us, we will work closely with you to determine if the patient meets criteria for either the classic or variant form of CJD (*See Attachment 1 "Diagnostic Criteria for CJD" and Attachment 2 "Diagnostic Criteria on variant CJD in the United States"*) and help arrange laboratory testing.

For suspect or confirmed cases of classic or vCJD, or other TSEs among New York City residents, please contact the Bureau of Communicable Disease during normal business hours:

TELEPHONE: 212-788-9830
FAX: 212-788-4268/5471 or 212-676-2688

Please also complete the New York City DOHMH's Universal Reporting Form using the code "TSE". Forms may be obtained by calling the Provider Access Line (PAL) 1-866-NYC-DOH1. Forms are also available on the DOHMH website at www.nyc.gov/html/doh as well as on the Health Alert Network (HAN). Please mail the completed form to:

New York City Department of Health and Mental Hygiene
Bureau of Communicable Disease
125 Worth Street, Room 315, CN6
New York, New York 10013

CJD and vCJD, as well as any diagnosis of dementia, is also reportable to the New York State Department of Health's Alzheimer's Disease and Other Dementias Registry under Article 20 of the New York State Public Health Law enacted in January 1, 1987. To avoid the need for dual reporting of patients with a suspect or confirmed TSE, we ask that you notify the New York City DOHMH and we will immediately share that information with the New York State Department of Health. Reporting of dementia not associated with TSE should be reported directly to the New York State Department of Health's Alzheimer's Disease and Other Dementias Registry.

Free Diagnostic Laboratory Testing for Prion Related Disease is Available at Case Western

University: Since a confirmatory diagnosis of these diseases requires pathologic examination of brain tissue, we strongly encourage you to arrange for a post-mortem examination for fatal cases with clinical syndromes consistent with classic or vCJD. If a pre-mortem brain biopsy is performed, we urge you to submit both frozen and fixed biopsy tissue for testing, similar to the protocol for autopsy tissue.

The CDC, in conjunction with the American Association of Neuropathologists, has established a National Prion Disease Pathology Surveillance Center at the Division of Neuropathology at Case Western Reserve University in Cleveland, Ohio. Pathologic examinations are conducted to monitor the incidence of 1) vCJD, 2) iatrogenic CJD acquired from contaminated surgical instruments or other medical procedures, and 3) the possible occurrence of human prion disease acquired from elk or deer affected by chronic wasting disease.

The National Prion Disease Pathology Surveillance Center performs histopathology, immunohistochemistry and Western blot on autopsy and biopsy tissues to determine the presence, distribution and type of protease-resistant or scrapie prion protein. In addition, this center performs prion protein gene sequencing to determine the presence of pathogenic mutations. Cerebrospinal fluid (CSF) is also examined for the presence of the CJD protein marker 14-3-3. Test results are reported in a timely manner and are free of charge to the sender of the sample.

Tests performed by the National Prion Disease Pathology Surveillance Center

Test on biopsy tissue	Turn-around-times
Western Blot of the prion protein (PrP). (Establishes presence and type of scrapie PrP; frozen tissue required)	3 – 5 working days
Histology and PrP immunohistochemistry. (Establish presence and distribution of scrapie PrP on fixed tissue)	5 working days
14-3-3 determination in CSF	3 – 5 working days
Tests on autopsy tissues	Turn-around-times
Western Blot of PrP	3 weeks
Histology and immunohistochemistry of PrP	3 weeks
PrP gene sequencing. (Identifies mutations and codon 129 genotype needed for precise prion disease type diagnosis)	3 – 4 weeks (biopsies and autopsies)
Summary report with prion disease type diagnosis based on all above tests	4 – 5 weeks (biopsies and autopsies)

National Prion Disease Pathology Surveillance Center Data (1997-2003)

Year	Referrals	Total Prion Disease	Sporadic	Familial	Iatrogenic	vCJD
1997	104	60	54	6	0	0
1998	94	51	44	6	1	0
1999	114	74	65	9	0	0
2000	169	111	97	12	2	0
2001	247	154	138	16	0	0
2002	265 ¹	151	127	22	1	1 ²
2003 ³	228	131 ⁴	61	10	1	0
Total	1221	732 (60%)	586	81	5	1

¹ Includes 2 inconclusive cases; ² Acquired in United Kingdom, living; ³ Through November 2003

⁴ final diagnoses for 59 of the 131 prion cases are pending but vCJD has been ruled out

Information regarding the laboratory tests, specimen collection protocols and shipping instructions can be obtained by calling the National Prion Disease Pathology Surveillance Center at (216) 368-0587 or via their Website at www.cjdsurveillance.com.

Importance of Performing Autopsies on Any Suspect Case:

We strongly encourage you to discuss the importance of autopsy for confirming the diagnosis with the patient's family in all cases of rapidly progressing dementia consistent with CJD. The autopsy may be limited to the brain. The National Prion Disease Pathology Surveillance Center can help make arrangements for autopsies by paying for the autopsy and transportation of the body, when necessary, and for tissue shipment.

Given the public health importance of confirming the diagnosis in any patient suspected to have the variant form of CJD, the Office of the Chief Medical Examiner will perform autopsies on all suspect vCJD cases without a pre-mortem pathologic diagnosis. Fatal cases with suspected vCJD should be reported immediately to the Office of the Chief Medical Examiner at 212-447-2030. The DOHMH and the Office of the Chief Medical Examiner will work with you to ensure that an autopsy examination is performed for any suspect cases of CJD or TSE aged less than 55 years, given the potential public health importance of a confirmed vCJD case in New York City.

CJD Surveillance Findings in New York City since 2001:

We have received 39 reports of suspected cases of CJD since TSEs were made reportable in July 2001. These include 28 cases reported by laboratories, including the National Prion Disease Pathology Surveillance Center and Quest laboratories which perform testing for the 14-3-3 protein, as well as six cases identified through death certificate surveillance (records listing CJD among the contributing factors). Four cases were identified through the New York State DOH Alzheimers and Other Dementias Registry. We received very few reports from individual practitioners or medical facilities, all of which had already been identified through laboratory surveillance.

Of the 39 reports, 22 were for New York City residents; the others were non-New York City residents seeking care at a New York City hospital. Of these 22, six were considered to have definite CJD through pathologic examination of biopsy/autopsy material. Ten were classified as probable or possible cases based on meeting clinical criteria (See Attachments). This incidence of approximately 0.7/million is less than the expected annual incidence of one case per million population. It is not clear if this is the result of limited testing and/or under reporting or the true incidence of CJD in New York City. Thus far, no vCJD has been identified to date

In summary, we encourage all providers in New York City who are caring for patients with suspected CJD or other TSEs, to notify the New York City DOHMH as soon as possible after the diagnosis is first considered so that we can assist in establishing the diagnosis. We also encourage providers to discuss the issue of autopsy with the patient's family, when appropriate, so that arrangements can be made at the time of death for testing at the National Prion Disease Pathology Surveillance Center.

Patient's 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 and healthcare professionals. 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,

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

(Global Surveillance, Diagnosis, and Therapy of Human Transmissible Spongiform Encephalopathies: Report of a WHO Consultation, February 9-11, 1998, Geneva, Switzerland)

1. 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/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 human cadaveric-derived pituitary hormone; 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.

Attachment 2: Diagnostic Criteria for Variant Creutzfeldt-Jakob Disease in the United States

Definite Variant CJD: Neuropathologic examination of brain tissue is required to confirm a diagnosis of variant CJD. 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 Variant CJD: 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 onset 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 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 variant CJD 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.