

# Creutzfeldt-Jakob Disease

## **DISEASE REPORTABLE WITHIN 24 HOURS OF DIAGNOSIS**

Per N.J.A.C. 8:57, health care providers and administrators shall report by mail or by electronic reporting within 24 hours of diagnosis, confirmed cases of Creutzfeldt-Jakob disease to the health officer of the jurisdiction where the ill or infected person lives, or if unknown, wherein the diagnosis is made. A directory of local health departments in New Jersey is available at

<http://www.state.nj.us/health/lh/directory/lhdselectcounty.shtml>.

If the health officer is unavailable, the health care provider or administrator shall make the report to the Department by telephone to 609.826.5964, between 8:00 A.M. and 5:00 P.M. on non-holiday weekdays or to 609.392.2020 during all other days and hours.



## 1 THE DISEASE AND ITS EPIDEMIOLOGY

### A. Etiologic Agent

Creutzfeldt-Jakob disease (CJD) is part of a group of human and animal diseases called transmissible spongiform encephalopathies (TSEs). TSEs are believed to be caused by an unconventional, infectious agent called a prion that is able to induce abnormal folding of normal cellular prion proteins in the brain, leading to brain damage and other signs and symptoms characteristic of TSEs. Prion diseases are usually rapidly progressive and always fatal.

Five prion diseases occur in humans: Gerstmann-Straussler-Scheinker syndrome, kuru, fatal familial insomnia, CJD (including the major categories of sporadic, inherited/familial, and iatrogenic), and new variant CJD (nvCJD).

### B. Clinical Description and Laboratory Diagnosis

CJD has an insidious onset with confusion and forgetfulness that progress rapidly to severe cortical dementia in combination with ataxia, myoclonus, akinetic mutism, and an abnormal electroencephalogram (EEG). Death usually occurs in under a year (average four months) and there is no known treatment or cure. Routine laboratory studies of cerebrospinal fluid (CSF) are generally negative with the exception of mildly elevated protein. The presence of 14-3-3 protein, a protein that is released by damaged or dying nerve cells, in the CSF of symptomatic cases supports a diagnosis of CJD. However, false negatives generated by testing early during the disease course and false positives associated with herpes encephalitis, hypoxic brain damage, acute stroke, and other conditions have been reported.

### C. Reservoirs

Humans constitute the only known reservoir of sporadic, inherited/familial, and iatrogenic CJD. However, in the case of nvCJD, there is mounting evidence to support that cattle infected with bovine spongiform encephalopathy (BSE) might be a reservoir.

#### **D. Modes of Transmission**

Sporadic CJD is not transmitted via the airborne route nor is there evidence to suggest that it is transmitted through person-to-person contact; the exact mode of transmission associated with sporadic CJD is unknown. In the familial form of CJD there is an inherited mutation in the normal prion protein gene that seems to make conversion into the abnormal form more likely. Iatrogenic CJD transmission can occur through contaminated pharmaceutical preparations and surgical instruments. Thus far, cases of iatrogenic CJD have been reported in association with contaminated corneal transplants, dura mater grafts, neurosurgical equipment, and pituitary-derived human growth hormone. Precautions are now in place to ensure that these modes of transmission do not occur. The nvCJD has been linked to consumption of certain parts of cattle infected with the agent causing BSE and possibly with receipt of contaminated human blood or blood products from nvCJD-infected blood donors.

#### **E. Incubation Period**

The incubation period of sporadic and familial CJD can be years to decades. The incubation period associated with iatrogenic cases ranges from 15 months to possibly 30 years. The incubation period of nvCJD is unclear; some researchers postulate a five-year incubation period, while others postulate a much longer incubation period, similar to that of sporadic CJD.

#### **F. Period of Communicability or Infectious Period**

CJD is not directly communicable from person to person. However, medical equipment may become contaminated during neurosurgical procedures as tissues of the central nervous system are infectious throughout the period that CJD patients are symptomatic.

#### **G. Epidemiology**

Cases of sporadic CJD have been documented since it was first clinically described in the 1920s. However, the unconventional etiologic agent, called a “prion” (which is found in all CJD cases), was not identified until the 1980s. Sporadic CJD, which accounts for 85% of the cases, is reported worldwide with an annual incidence rate of approximately one case per 1 million population. Sporadic CJD occurs almost exclusively (99%) in patients 35 years and older, and the average age of onset for sporadic cases is 68 years. Familial CJD, which accounts for 10% to 15% of the cases, has an average age of onset approximately ten years younger than sporadic CJD. Iatrogenic CJD comprises less than 5% of the overall cases; the epidemiological findings associated with iatrogenic CJD vary according to the source of exposure. In New Jersey, an annual average of seven cases of sporadic CJD is reported to the New Jersey Department of Health and Senior Services (NJDHSS), with a range of 3 to 14 cases in any given year. Differences in the number of cases identified are due to fluctuations in surveillance and reporting. Familial CJD accounts for approximately 14% of the cases. There have been no iatrogenic or nvCJD cases identified in New Jersey.

The nvCJD was first identified in the United Kingdom in 1996 and is associated with BSE, commonly referred to as “mad cow disease” in the popular press. The nvCJD and sporadic CJD are not the same disease. The epidemiological findings associated with nvCJD are

notably different from that of sporadic CJD. The nvCJD occurs primarily in younger individuals, with an average age of onset of 27 years (range 16 to 48 years) and the duration of symptoms for nvCJD is longer than sporadic CJD, with a somewhat protracted course of illness lasting approximately 16 months. Also, nvCJD is not associated with typical periodic complexes on the EEG; instead, relatively specific changes may be seen using magnetic resonance imaging (MRI). Both forms can be distinguished when biopsy or postmortem examination of brain is performed. Over 200 cases of nvCJD have been reported worldwide since 1996, with the majority of the cases exposed while the case-patients were residing or staying in Europe, including the United Kingdom. To date, three cases of nvCJD have been diagnosed in the United States; two of the cases were linked to exposure in the United Kingdom and one case was linked to exposure in Saudi Arabia.

## **2 NEW JERSEY DEPARTMENT OF HEALTH AND SENIOR SERVICES CASE DEFINITION**

### **A. Clinical Description**

Clinical symptoms include rapidly progressing dementia accompanied by one or more of the following: myoclonus, visual or cerebellar problems, pyramidal or extrapyramidal features, and akinetic mutism. Duration of illness is less than two years.

### **B. Laboratory Criteria and Case Classification**

In addition to the three case classifications listed below, cases of CJD are classified according to mode of transmission: sporadic, familial, iatrogenic, or new variant.

#### **CONFIRMED**

A clinically compatible case supported by postmortem exam or brain biopsy, with identification of CJD by one or more of the following:

- Standard neuropathological techniques, AND/OR
- Immunohistochemical brain examination, AND/OR
- Western-blot confirmed protease-resistant prion protein, AND/OR
- Presence of scrapie-associated fibrils conducted on brain tissue

#### **PROBABLE**

A clinically compatible case without postmortem exam or brain biopsy, accompanied by at least one of the following diagnostic aids (tests are suggestive but not specific for CJD):

- Characteristic EEG changes (CJD), AND/OR
- Detection of 14-3-3 protein in cerebrospinal fluid (CJD), AND/OR
- Characteristic posterior thalamic high signal on MRI scan (nvCJD only), AND/OR
- Positive tonsil biopsy (nvCJD only)

**POSSIBLE**

A clinically compatible case not supported by laboratory findings, EEG, or MRI, with a recognized epidemiological, familial, or iatrogenic risk factor.

**C. Differences from Centers for Disease Control and Prevention Case Definition**

There is no official Centers for Disease Control and Prevention (CDC) case definition for CJD. It is not a nationally notifiable disease. The NJDHSS case definition is based on the World Health Organization (WHO) case definition for prion disease and CDC experts assisted NJDHSS Infectious and Zoonotic Diseases Program (IZDP) epidemiologists in the development of the New Jersey case definition.

## **3 LABORATORY TESTING AVAILABLE**

Laboratory diagnosis is based on analysis of CSF, blood, and brain tissue obtained at either biopsy or autopsy. The National Prion Disease Pathology Surveillance Center (NPDPSC), established in 1997 at the Division of Neuropathology of Case Western Reserve University, conducts testing for CJD. The NPDPSC is the only laboratory in the United States that offers testing for CJD and they will coordinate postmortem examinations free of charge. The NPDPSC recommends that postmortem examinations be scheduled as soon as possible after death; however, the brain tissue can be examined 48 to 72 hours postmortem, especially if the body is refrigerated. Additional information about the NPDPSC, with specific instructions on how to collect and ship specimens, and autopsy FAQs can be found on their Web site at <http://www.cjdsurveillance.com> or by calling the NPDPSC Autopsy Coordinator at 216.368.0587.

The NJDHSS Public Health and Environmental Laboratories and the CDC do not provide testing of clinical specimens for CJD.

## **4 PURPOSE OF SURVEILLANCE AND REPORTING AND REPORTING REQUIREMENTS**

**A. Purpose of Surveillance and Reporting**

- To provide information about CJD, its transmission, and methods of prevention
- To promptly identify clusters or outbreaks of CJD
- To identify transmission sources of public health concern (e.g., food supply, organ transplants, blood products, medical procedures)
- To quickly identify suspect cases and provide resources for clinicians and family members, such as postmortem examination for case confirmation

## **B. Laboratory Reporting Requirements**

The New Jersey Administrative Code (NJAC 8:57-1.8) stipulates that laboratories report (by telephone, confidential fax, over the Internet using the confidential and secure Communicable Disease Reporting and Surveillance System [CDRSS], or in writing) all cases of CJD to the local health officer having jurisdiction over the locality in which the patient lives or, if unknown, to the health officer in whose jurisdiction the healthcare provider requesting the laboratory examination is located.

## **C. Healthcare Provider Reporting Requirements**

The New Jersey Administrative Code (NJAC 8:57-1.4) stipulates that healthcare providers report (by telephone, confidential fax, or in writing) all cases of CJD to the local health officer having jurisdiction over the locality in which the patient lives or, if unknown, to the health officer in whose jurisdiction the healthcare provider requesting the laboratory examination is located. The report shall contain the name of the disease; date of illness onset; and name, age, date of birth, race, ethnicity, home address, and telephone number of the person they are reporting. In addition, name, address, institution, and telephone number of reporting official should be reported.

## **D. Health Officer's Reporting and Follow-up Responsibilities**

The New Jersey Administrative Code (NJAC 8:57-1.7) stipulates that each local health officer must report the occurrence of any case of CJD within 24 hours of receiving the report. Written or electronic copies of the reports must be made to NJDHSS and may be submitted over the Internet using the confidential and secure CDRSS.

# **5 CASE INVESTIGATION**

## **A. Forms and Laboratory Reports**

It is requested that the local health officer complete a CDS-8 CJD case investigation form, which can be found online at <http://www.state.nj.us/health/forms/cds-8.pdf>, by interviewing the clinician, patient, and others who may be able to provide pertinent information. Much of the information required on the form can be obtained from the patient's healthcare provider or the medical record. For cases occurring in individuals under age 55, additional investigation may be warranted to identify any potential risk factors for familial, iatrogenic, or nvCJD.

Whenever possible, the local health department (LHD) should work with the clinician to provide information about obtaining postmortem examination for case confirmation and other diagnostic aids available at the NPDPS (refer to section 3). When applicable, the LHD should also provide information about infection control guidelines to hospitals or funeral directors (refer to section 6B).

**B. Entry into CDRSS**

The mandatory fields in CDRSS include disease, last name, county, municipality, gender, race, ethnicity, case status, and report status.

The following table can be used as a quick reference guide to determine which CDRSS fields need to be completed for accurate and complete reporting of CJD. The “Tab” column includes the tabs that appear along the top of the CDRSS screen. The “Required Information” column provides detailed explanations of what data should be entered.

<b>CDRSS Screen</b>	<b>Required Information</b>
<b>Patient Info</b>	Enter the disease name (“CREUTZFELDT-JAKOB DISEASE”), patient demographic information, illness onset date, and the date the case was reported to the LHD. Select a subgroup (“SPORADIC,” “FAMILIAL,” “IATROGENIC,” “NEW VARIANT” or “UNKNOWN”) according to the mode of transmission (refer to section 2B).
<b>Addresses</b>	Enter any alternate address (e.g., rehabilitation facility). Use the “Comments” section in this screen to record any pertinent information about the alternate address (e.g., length of stay at rehabilitation facility). Entering an alternate address will allow other disease investigators access to the case if the alternate address falls within their jurisdiction. Cases reported to NJDHSS by the NPDpsc do not have patient address information. As such, NJDHSS will assign these cases to the LHD where the ordering physician’s office is located. If, during the course of an investigation, a case is found to reside outside of the LHD’s jurisdiction, that information should be recorded in the “Comments” section and the pending case will be transferred to the appropriate municipality.
<b>Clinical Status</b>	Enter any treatment that the patient received and record the names of the medical facilities and physician(s) involved in the patient’s care. If the patient received care from two or more hospitals, be sure that all are entered so the case can be accessed by all infection control professionals (ICPs) covering these facilities. If the patient died, date of death should be recorded under the “Mortality” section.
<b>Signs/Symptoms</b>	Check appropriate boxes for signs and symptoms and indicate their onset. Make every effort to get complete information by interviewing the physician, family members, ICP, or others who might have knowledge of the patient’s illness. Also, information regarding the resolution of signs and symptoms should be entered.

CDRSS Screen	Required Information
<b>Risk Factors</b>	Enter complete information about risk factors, including travel to the United Kingdom or Europe for greater than six months, familial history of dementia, blood and/or organ donation, recipient of blood and/or organ donation, and history of exposure to potentially contaminated neurosurgical equipment (e.g., corneal transplant, dura mater grafts, or human-derived growth hormone).
<b>Laboratory Eval</b>	All laboratory test results for CJD should be entered by selecting “NATIONAL PRION DISEASE SURVEILLANCE CENTER” under laboratory name. For all 14-3-3 positive or ambiguous tests, select “14-3-3” and “CSF.” In the “TEST RESULT” field select “POSITIVE/REACTIVE” for positive results or “EQUIVOCAL” for ambiguous results. Also record “AMBIGUOUS” in the “LABORATORY COMMENTS” section. For all WB and IHC positive tests, select “WB” or “IHC” and “BRAIN TISSUE.” In “TEST RESULT” field select “POSITIVE/REACTIVE” and record the specific findings of the postmortem or brain biopsy analysis in the “LABORATORY COMMENTS” section. If arrangements have been made to send postmortem tissue to the NPDPSA but the patient has not expired, document this information in the “LABORATORY COMMENTS” section.
<b>Contact Tracing</b>	Information regarding contacts is not required for this disease.
<b>Case Comments</b>	Enter general comments (i.e., information that is not discretely captured by a specific topic screen or drop-down menu) in the “COMMENTS” section. <b>NOTE:</b> Select pieces of information entered in the “COMMENTS” section CANNOT be automatically exported when generating reports. Therefore, whenever possible, record information about the case in the fields that have been designated to capture this information; information included in these fields CAN be automatically exported when generating reports.
<b>Epidemiology</b>	Record name of and contact information for case investigators from other agencies (e.g., CDC, out-of-state health departments). Document communication between investigators in the “COMMENTS” section.

CDRSS Screen	Required Information
<p><b>Case Classification Report Status</b></p>	<p>Case status options are “REPORT UNDER INVESTIGATION (RUI),” “CONFIRMED,” “PROBABLE,” “POSSIBLE,” and “NOT A CASE.”</p> <ul style="list-style-type: none"> <li>• All NPDPSK cases entered by NJDHSS will be assigned a case status of “REPORT UNDER INVESTIGATION (RUI).”</li> <li>• Cases still under investigation by the LHD should be assigned a case status of “REPORT UNDER INVESTIGATION (RUI).”</li> <li>• Upon completion of the investigation, the LHD should assign a case status on the basis of the case definition.</li> </ul> <p>Report status options are “PENDING,” “LHD OPEN,” “LHD REVIEW,” “LHD CLOSED,” “DELETE,” “REOPENED,” “DHSS OPEN,” “DHSS REVIEW,” and “DHSS APPROVED.”</p> <ul style="list-style-type: none"> <li>• All NPDPSK cases entered by NJDHSS will be assigned a report status of “PENDING.”</li> <li>• Once the LHD begins investigating a case, the report status should be changed to “LHD OPEN.”</li> <li>• The “LHD REVIEW” option can be used if the LHD has a person who reviews the case before it is closed (e.g., health officer or director of nursing).</li> <li>• Once the LHD investigation is complete and all the data are entered into CDRSS, the LHD should change the report status to “LHD CLOSED.”</li> <li>• “LHD CLOSED” cases will be reviewed by DHSS and be assigned one of the DHSS-specific report status categories. If additional information is needed on a particular case, the report status will be changed to “REOPENED” and the LHD will be notified by e-mail. Cases that are “DHSS APPROVED” cannot be edited by LHD staff (see section 5C below).</li> </ul> <p>If a case is inappropriately entered (e.g., a case of a different reportable disease entered under CJD) the case should be assigned a report status of “DELETE.” A report status of “DELETE” should NOT be used if a reported case of CJD simply does not meet case definition. Rather, it should be assigned the appropriate case status, as described above.</p>

**C. Other Reporting/Investigation Issues**

1. Case report forms (e.g., CDS-8 and laboratory report forms) DO NOT need to be mailed to NJDHSS as long as mandatory fields in CDRSS indicated in section 5B are completed.

2. Once the LHD completes its investigation and assigns a report status of “LHD closed,” NJDHSS will review the case. NJDHSS will approve the case by changing the report status to “DHSS approved.” At this time, the case will be submitted to CDC and the case will be locked for editing. If additional information is received after a case has been placed in “DHSS approved,” you will need to contact NJDHSS to reopen the case. This should be done only if the additional information changes the case status of the report.
3. Every effort should be made to complete the investigation within three months of opening a case. Cases that remain open for three months or more and have no investigation or update notes will be closed by NJDHSS and marked as not a case.

## **6 CONTROLLING FURTHER SPREAD**

### **A. Isolation and Quarantine Requirements (NJAC 8:57-1.10)**

#### **Minimum Period of Isolation of Patient**

Because CJD is not transmitted from person to person, there are no restrictions for case-patients.

#### **Minimum Period of Quarantine of Contacts**

There are no restrictions of contacts.

### **B. Protection of Contacts of a Case**

CJD is not transmitted through person-to-person contact and there are no special situations or precautions for case contacts. However, certain body fluids, including brain, spinal cord, and cornea materials, are considered potentially infectious. As such, two situations may require special consideration: suspect cases of CJD undergoing neurosurgical procedures and confirmed cases being embalmed before burial or cremation. If CJD is suspected in the differential diagnosis, the CDC and World Health Organization recommend implementing TSE infection control precautions prior to and immediately preceding any neurosurgical procedure. Specific guidelines, including disinfectants and categories of infectious materials, can be found at [http://whqlibdoc.who.int/hq/2000/WHO\\_CDS\\_CSRAPH\\_2000.3.pdf](http://whqlibdoc.who.int/hq/2000/WHO_CDS_CSRAPH_2000.3.pdf). If CJD is confirmed through autopsy, contact precautions must be followed during embalming.

### **C. Managing Special Situations**

#### **Locally Acquired Case**

Isolated cases of sporadic and familial CJD are not unusual. If it is suspected that a case was acquired through iatrogenic exposure, it may be necessary to investigate local risk factors or to conduct surveillance for other people who may have been exposed. In addition, for cases that occur in individuals under age 55, it is important for the LHD to gather accurate and

complete information about exposure, family history of dementia or CJD, and clinical signs and symptoms.

### **Reported Incidence Is Higher Than Usual/Outbreak Suspected**

If the number of reported cases in a setting or town/community is higher than usual, or if an outbreak is suspected, please contact IZDP at 609.588.7500 immediately. This situation may warrant an investigation of the clustered cases to determine a course of action to prevent further cases. IZDP staff can perform surveillance for clusters of illness that may cross several jurisdictions and therefore be difficult to identify at a local level.

## **7 PREVENTIVE MEASURES**

### **Environmental Measures**

Because some cases of iatrogenic CJD have been associated with certain medical procedures, policies have been set into place to prevent these sorts of cases from happening. For example, surgical instruments used on the brain or nervous tissue of someone with suspected CJD are destroyed or quarantined until a diagnosis is confirmed. In addition, to help protect the nation's blood supply, people with risk of exposure to CJD and nvCJD are not eligible to donate blood. The risk of contracting nvCJD in the United States remains extremely low, as numerous precautions are in place to prevent BSE-infected cattle and tissue from entering the human food supply. Of the three nvCJD cases reported from the United States, strong evidence suggests all three cases were acquired abroad.

### **Personal Preventive Measures**

There is no known way to prevent sporadic CJD from developing. People with a family history of neurological disease may benefit from talking with a genetics counselor, who can help decide if genetic testing for CJD may be appropriate.

### **Additional Information**

A CJD Fact Sheet is available at the NJDHSS Web site at <http://www.state.nj.us/health/cd/>.

Additional information can be found on the CDC Web site at <http://www.cdc.gov/ncidod/dvrd/cjd/>.

Resources for cases and family members can be found at the CJD Foundation at <http://www.cjdfoundation.org>.

Autopsy and laboratory testing information can be found at the NPDPS at <http://www.cjdsurveillance.com>.

## References

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