

Prion Diseases

Organism: Prion diseases (PDs) or transmissible spongiform encephalopathies (TSEs) – family of rare progressive neurodegenerative disorders that affect both humans and animals with long incubation periods and pathologically characteristic spongiform changes associated with neuronal loss and absence of inflammatory response. Causative agent believed to be a prion – abnormal, transmissible agent able to induce abnormal folding of normal cellular prion proteins in brain, leading to brain damage and signs and symptoms of the disease. PDs are invariably fatal.

Incubation period: Highly variable, may be decades.

Infectious period: Not well characterized. See Table 1 for reports of transfusion-associated transmission from donors who were apparently well at the time of donation, but subsequently diagnosed with vCJD years later.

Transmission route: See Table 1.

Treatment: No specific treatment.

Information Needed for the Investigation

Verify the Diagnosis

Clinical picture: otherwise unexplained subacute progressive dementia and at least one of the following neurologic features – myoclonus, visual or cerebellar signs, pyramidal/extrapyramidal signs, or akinetic mutism. Signs and symptoms may vary depending on the PD.

Laboratory results: gold standard for diagnosis is pathological analysis of brain tissue at autopsy.

See attachment for WHO case definition for CJD; also pages 5-6 of the WA Dept of Health Surveillance and Reporting manual (<http://www.doh.wa.gov/Portals/1/Documents/5100/420-069-Guideline-Prion.pdf>), for definitions/criteria for other human PDs.

Determine the Extent of Illness

- Confirmed cases will be rare; Alaska should have <1 case/year. [US rate is ~1/million, increases to 3-4/million if looking at older age groups.] However, if several different reports are received in a seemingly short period of time, consult with CDC about the need for a cluster-type analysis.
- For different scenarios, follow steps in Table 2 below.

Laboratory Specimens

- Consult with the National Prion Disease Pathology and Surveillance Center for assistance in obtaining an autopsy (see Table 3). Most likely referral is to Dr. Montine at Harborview in Seattle. However, NPDPS also has a pathologist who will travel to Alaska if an appropriate facility is available.

- Recommend clinician consult with CDC/experts if they are looking for specific details on interpreting diagnostics or patient status.

Hospital Considerations

- Use Standard Precautions for patient.
<http://www.cdc.gov/hicpac/2007IP/2007isolationPrecautions.html>
- The World Health Organization (WHO) has developed [CJD infection control guidelines](#) that can be a valuable guide to infection control personnel and other health care workers involved in the care of CJD patients. Destruction of heat-resistant surgical instruments that come in contact with high infectivity tissues, albeit the safest and most unambiguous.
http://www.who.int/csr/resources/publications/bse/WHO_CDS_CSRAPH_2000_3/en/
- Centers for Disease control and Prevention Guidelines can be found at
http://www.cdc.gov/ncidod/dvrd/cjd/qa_cjd_infection_control.htm#reprocessed
- All disposable instruments, materials, and wastes that come in contact with high infectivity tissues (brain, spinal cord, and eyes) and low infectivity tissues (cerebrospinal fluid, kidneys, liver, lungs, lymph nodes, spleen, and placenta) of suspected or confirmed TSE patients should be disposed of by incineration.
- Surfaces and heat-sensitive re-usable instruments that come in contact with high infectivity and low infectivity tissues should be decontaminated by flooding with or soaking in 2N NaOH or undiluted sodium hypochlorite for 1 hour and rinsed with water.
- An autopsied or traumatized body of a suspected or confirmed CJD patient can be embalmed, using the precautions outlined in the WHO [CJD infection control guidelines](#). CJD patients who have not been autopsied or whose bodies have not been traumatized can be embalmed using Standard Precautions. Family members of CJD patients should be advised to avoid superficial contact (such as touching or kissing the patient's face) with the body of a CJD patient who has been autopsied. However, if the patient has not been autopsied, such contact need not be discouraged.

Contact and Control Measures

- None indicated.
- Some of these cases have caused media inquiries and community concern; consider the need for educational materials.

Reporting Requirements

- FTR: write up cluster investigations
- Morbidity Database: enter all *confirmed* and *probable* cases.
- WHO Case Definition is used to define *confirmed* and *probable* cases; see attached description.

Table 1. Type of Prion Diseases

Sporadic	Sporadic Creutzfeldt-Jakob Disease (sCJD)	<ul style="list-style-type: none"> • Most common of the human prion diseases, ~85% of all cases. • Five distinct types that differ clinically (observable physical and subjective symptoms) and neuropathologically (tissue changes in brain). • Molecular features of types also vary, e.g., genotype at codon 129 of prion protein gene, length of the scrapie prion protein.
	Sporadic Fatal Insomnia (sFI)	<ul style="list-style-type: none"> • Clinical and histopathological features indistinguishable from those of FFI but does not have mutation on the prion gene that characterizes FFI.
Familial	Familial CJD (fCJD)	<ul style="list-style-type: none"> • Second most common type of CJD, ~10-15% of cases worldwide. • Caused by genetic mutation in the prion protein gene, which causes a change in the amino acid sequence of the normal prion protein; change believed to cause mutated prion protein to take on scrapie prion protein conformation. • DNA extracted from blood or brain tissue obtained at biopsy or autopsy may be used to test for mutations in persons with suspected fCJD. • Currently, 55+ mutations of the prion gene are known to cause fCJD and other familial prion diseases in humans, including FFI and GSS.
	Fatal Familial Insomnia (FFI)	
	Gerstmann -Sträussler-Scheinker disease (GSS)	
Iatrogenic	Iatrogenic CJD (iCJD)	<ul style="list-style-type: none"> • Form of acquired CJD, <1% of cases. • Both lab/clinical research determined that human-to-human transmission can occur as the result of tissue implant, use of contaminated neurosurgical instruments, or administration of human hormones extracted from cadavers. • Although blood transmission of CJD reported only in vCJD, American Red Cross currently defers donors with a history of permanence in certain foreign countries or family history of CJD.
	Variant CJD (vCJD)	<ul style="list-style-type: none"> • In 1996, the first cases reported in the UK; total cases worldwide ~200. • Strong evidence that vCJD was acquired from consuming cattle affected by bovine spongiform encephalopathy, or “mad cow” disease, which occurred with epidemic proportions in the UK in the 1980s. • Cases in nations with no documented BSE have had exposures elsewhere (e.g., two US cases grew up outside the US). • vCJD has well defined and consistent clinical and pathological features that make it relatively easy to identify and distinguish from sCJD. vCJD is only type of PD in which definitive dx can be made with a biopsy of the tonsils. • Two vCJD cases acquired via blood transfusion reported in the UK; blood was extracted from persons with vCJD prior to their diagnosis.
	Kuru	<ul style="list-style-type: none"> • Acquired PD that is virtually extinct. • Originally described in members of a native tribe in New Guinea known to practice cannibalism; epidemics probably originated from the consumption of infected meat from a member of the tribe affected by sporadic CJD. • Clinically and pathologically, Kuru is fairly different from vCJD.

Table 2: Scenarios that might occur

Scenario	Investigation needed	Recommendations
Health care provider (HCP) from outside AK treating an AK patient reports a suspected or confirmed PD case	<ul style="list-style-type: none"> • If dx is confirmed, complete case report form based on medical record and clinician interview. • Alert PHNs of cases in their region. 	<ul style="list-style-type: none"> • Assume that proper diagnostics are being performed and that HCP is looped into NPDpsc.
HCP inside AK reports a suspected case	<ul style="list-style-type: none"> • If dx is confirmed, complete case report form based on medical record and clinician interview. • Alert PHNs of cases in their region. 	<ul style="list-style-type: none"> • Body should be referred for an autopsy. • Call NPDpsc to facilitate this; or have the HCP call directly.
PD case has been diagnosed; facility is calling because PD	<ul style="list-style-type: none"> • Consult with CDC about the appropriate follow-up. Facility staff (IP, risk managers, etc.) will need to make the 	

precautions may not have been followed	final decisions about notification of patients, but CDC and/or SOE can be part of those discussions.	
PD suspect has a POSITIVE 14-3-3 result	<ul style="list-style-type: none"> In general, NPDSPC staff conducts the follow-up on these test results to determine if a PD is still a likely diagnosis. If so, NPDSPC will contact SOE. 	<ul style="list-style-type: none"> If PDs are suspected, NPDSPC will work to ensure that an autopsy is obtained.

Table 3. Contacts

Name	Affiliation	Phone Number	Email address
Ermias Belay, MD	CDC	404-639-3091	eeb8@cdc.gov
Larry Schonberger, MD	CDC	404-639-4435	lbs1@cdc.gov
Ryan Maddox	CDC		zpz7@cdc.gov
James Sejvar, MD (neurologist)	CDC		zea3@cdc.gov
Tom Montine, MD (neuropath dept; most likely referral for autopsy)	Harborview Med Ctr, Seattle, WA	206-731-4106	tmontine@u.washington.edu
Pierluigi Gambetti, MD (director)	NPDSPC	216-368-0587	cjdsurv@po.cwru.edu
Sally Berri (manager)	NPDSPC	216-368-0819	sally.berri@case.edu
Kathy Lofy, MD	WA DOH	206-418-5500	kathy.lofy@doh.wa.gov

Resources

Websites:

1. NPDSPC: <http://www.cjdsurveillance.com>
2. CJD Foundation: www.cjdfoundation.org
3. CDC: <http://www.cdc.gov/ncidod/dvrd/cjd/>

Previous Regional Surveillance:

Through CDC, WA DOH gets funds to promote regional surveillance. Previously agreements had been with ID Dept of Health and Welfare, who had direct experience with managing cluster investigations, media interest in PDs, etc., and would be a good resource for those situations.

Contact Kris Carter: carterk1@dhw.idaho.gov.