# Prion Diseases:

## A Review for Linen Managers in Healthcare Facilities

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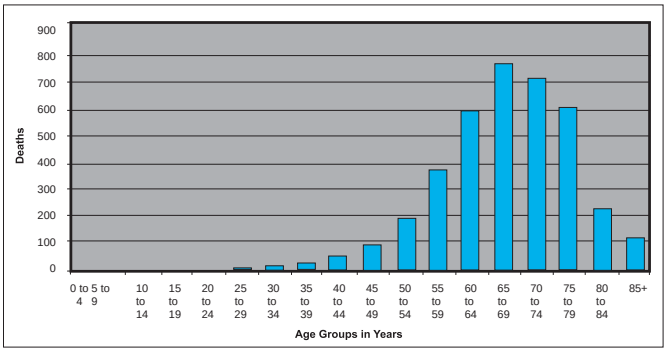
Control and prevention of infectious diseases is one of the most fascinating endeavors within public health because new infectious agents emerge and old diseases reinvent themselves. In 1996, for example, the world was alerted to a new disease in the United Kingdom (UK) affecting humans - Mad Cow disease.

In the months and years thereafter, we learned this disease was linked to consumption of beef from cows that were infected with bovine spongiform encephalopathy (BSE), and that the pathogen causing this disease was a prion. This development in the UK heightened public awareness of prion diseases in both man and animals around the world. As someone who works either in a healthcare facility (e.g., a hospital) or provides a service to such a facility, you may have heard about prion diseases. What exactly is a prion, what are prion diseases, and how does all this affect healthcare linen services and laundry?

### Epidemiology of Prion Diseases

Prion diseases are degenerative neurologic diseases that are universally fatal. That is, there is currently no known cure for this condition, and care of the patient is generally supportive. There are five prion diseases of humans, three of which are seen in the United States (US). These are Creutzfeldt-Jakob disease (CJD), fatal familial insomnia (FFI), and Gertsmann-Sträussler Scheinker disease (GSS). Of these, CJD is the most common - the incidence rate is one case (death) per one million population, or approximately 300 cases in the US annually. CJD occurs primarily in adults > 40 years of age, with peak incidence among persons in their 60's (Fig. 1). The onset of symptoms is insidious, starting with cognitive impairment (dementia) and sensory disturbances (visual failure), ataxia (loss of balance, instability) and progressing to myoclonus (jerking movements of the extremities when startled), and rigidity (Table 1). The course of illness is rapid, with death occurring approximately six months after onset. Towards the end of the clinical course, the patient is incapacitated, mute,

Figure 1. Creutzfeldt-Jakob Disease Deaths by Age Group, United States, 1979-1994




Source: Holman RC, Khan AS, Belay ED, Schonberger LB. Creutzfeldt-Jakob disease in the United States, 1979-1994: Using national mortality data to assess the possible occurrence of variant cases. *Emerg Infect Dis* 1996; 2 (4): 333-7.

Table 1. Clinical Signs and Symptoms of CJD

| Symptom | Present at Onset (%) | Present During Course (%) |
|---|---|---|
| Cognitive impairment | 69 | 100 |
| Cerebellar dysfunction | 33 | 71 |
| Visual failure | 18 | 42 |
| Myoclonus | 1 | 78 |
| Pyramidal disease | 2 | 62 |
| Extrapyramidal disease | 0.5 | 56 |
| Lower motor neuron signs | 0.5 | 12 |
| Seizures | 0 | 19 |

**N = 300 cases, 274 (78%) of which were sporadic CJD**

Source: Brown PA, Gibbs CJ, Rodgers-Johnson P, et al. 1994; *Ann Neurol* 35: 513-29

with diminished ability to respond to stimuli. Death is largely due to pneumonia or other complicating conditions of dementia.

CJD is clinically different from other forms of dementia, including Alzheimer's disease and senile dementia, but the definitive diagnosis is made by histological examination of brain tissue. CJD causes vacuoles and spaces to form in brain tissue, giving the appearance of a "sponge." This characteristic histopathology is the basis of the clinical terminology for prion diseases - transmissible spongiform encephalopathies. CJD affected brain tissue does not show amyloid plaque formation, a characteristic that distinguishes CJD from Alzheimer's disease. The diagnosis of CJD is made primarily via biopsy, but because the spongiform formations may not always be distributed uniformly throughout central nervous system tissue, the definitive diagnosis is often made at autopsy. Electroencephalogram (EEG) testing and a test for elevated levels of a specific protein (designated 14-3-3) in the spinal fluid are used to support the biopsy results. While not specific for CJD, the 14-3-3 protein in high concentrations is a marker for rapid neuron (nerve cell) death.

The vast majority (~ 90%) of CJD cases occurs as sporadic disease with no easily recognizable exposure event. Approximately 10% of cases are considered familial, where family history is considered as a risk factor. Less than 1% of cases are the result of medical intervention of some sort, including exposure to growth hormone (derived from pituitary) therapy, dura mater transplants, cornea transplants, and prion-contaminated neurosurgical instruments and devices. It was through the association of CJD disease with receipt of these biological materials and/or contact with inadequately sterilized instruments that we learned that CJD prions could be transmitted from one patient to others. Fortunately, many of these exposure opportunities have been drastically reduced due to surveillance and deferral of infected donors for transplant procedures and the move to recombinant resources for hormone derivatives. In the latter instance, use of recombinant resources all but eliminates the need for materials obtained directly from human donors.

**Clinical and Pathologic Characteristics Distinguishing Classic CJD from Variant CJD**

| Characteristic | Classic CJD | Variant CJD |
|---|---|---|
| Median age at death | 68 years | 28 years |
| Median duration of illness | 4-5 months | 13-14 months |
| Clinical signs and symptoms | Dementia; early neurologic signs | Prominent psychiatric/behavioral symptoms; painful dyesthesiasis; delayed neurologic signs |
| Periodic sharp waves on electroencephalogram | Often present | Often absent |
| "Pulvinar sign" on MRI* | Not reported | Present in > 75% of cases |
| Presence of "florid plaques" on neuropathology | Rare or absent | Present in large numbers |
| Immunohitochemical analysis of brain tissue | Variable accumulation | Marked accumulation of protease-resistance prion protein |
| Presence of agent in lymphoid tissue | Not readily detected | Readily detected |
| Increased glycoform ratio on immunoblot analysis of protease-resistance prion protein | Not reported | Marked accumulation of protease-resistance prion protein |

Source: Adapted from Belay E., Schonberger L. Variant Creutzfeldt-Jakob Disease and Bovine Spongiform Encephalopathy. Cin Lab Med 2002;22:849-62.

*An abnormal signal in the posterior thalami on T2- and difusion-weighted images and fluid-attenuated inversion recovery sequences on brain magnetic resonance imaging (MRI); in the appropriate clinical context, this signal is highly specific for vCJD.



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Although not strictly a category of classic CJD, variant CJD (vCJD, human BSE) is often mentioned when discussing human prion diseases. This disease can be distinguished from CJD in a number of ways. First, this disease originated in the UK in 1996 and a small number of cases have occurred primarily elsewhere in Europe. As of July 2005, there have been 184 cases of vCJD reported worldwide, including 161 cases in the UK, 13 in France, 3 cases in Ireland, and 1 case each in Canada, Italy, Japan, The Netherlands, Saudi Arabia, and the US. The one case in the US presumably had been exposed to infected beef while living in the UK. Cases in some of the other countries mentioned may have been due to consumption of imported infected beef from the UK. The clinical course of vCJD is longer compared to that of classic sporadic CJD (symptoms can persist for 1 - 2 years). vCJD can affect younger people - the age range of vCJD patients in the UK is 16 - 48 years, with the median age being 28. Table 2 compares and contrasts classic sporadic CJD with vCJD, focusing on signs and symptoms and diagnostic test results.

**What Are Prions, and Where Do You Find Them?**

Our natural inclination, given all the discussion of prion diseases as transmissible conditions, is to think of prions as infectious agents acquired from extraneous sources, that is from somewhere or something apart from us. Currently, the consensus is that prions are composed of protein without genetic material.

"Prion" was coined from the concept of a protein acting as an infectious agent. Interestingly, prions are derived from a normal component of our cells, with large concentrations of this normal protein located in CNS tissues and in lesser amounts in other organ systems and tissues. The gene that encodes the normal prion, or PrPc, is located on chromosome 20. The normal PrPc has a conformation or 3D structure that we designate as "alpha."

A trigger event as yet unknown causes this protein to become misshapened and convert to a totally different conformation known as "beta," characterized as a folded, accordion-like structure. Once this conversion has occurred, the abnormal prion, or PrPres (indicates protein resistant to proteinase K digestion), serves as a template with which all the neighboring PrPc proteins are converted to the abnormal conformation.

It is believed that prion disease symptoms become evident once a critical mass of the PrPres is reached, and this may require many years to get to this state. One theory hypothesizes that a random mutation in the gene that encodes PrPc may help to explain why there are so few cases of CJD and the vast majority appear to arise spontaneously.

Prions (PrPres) are not found throughout the body in tissues and fluids in equal concentrations. Table 3 shows the distribution of prion concentration and risk assessment category assigned to various tissues and organs. It is evident that the greatest concentration of prions is found in the brain and tissues of the CNS. Interestingly, many tissues and fluids including blood have low to no risk of transmission associated with them.

Table 3. Risk of CJD Transmission as a Function of Type of Tissue and Expected Relative Concentration of CJD Agent.

| Risk | Tissue |
|---|---|
| High (1) | Brain, dura mater, cornea |
| Medium (2) | Cerebrospinal fluid, kidney, liver, lymph nodes, spleen |
| Low to None (3) | Blood, urine, adrenal gland, feces, heart, bone marrow, muscle, nasal mucus, peripheral nerves, saliva, gingival, sputum, tears |

Adapted from Geerstma R, The Netherlands, 1995; Asher D, Bethesda, 1996; Brown P, Bethesda, 1996.

1: More that 50% of CJD infectivity tests positive
2: 4 - 40% of CJD infectivity tests positive
3: Infectivity tests negative

The observation that blood is a poor source of exposure for classic sporadic CJD comes from studies examining the incidence of CJD in the general population and comparing this rate with that for highly-transfused persons (e.g., hemophiliacs). Hemophiliacs have approximately the same incidence of CJD as the general population. Recent reports from the UK, however, have noted that vCJD may be possibly transmitted via blood transfusions. This stands in stark contrast to what we know for classic sporadic CJD; again, no cases of vCJD have occurred in the US without travel or residence history in the UK, and no cases of classic CJD have been linked to blood transfusion.

As mentioned previously, less than 1% of classic CJD cases have been linked to medical intervention events such as selected tissue transplant procedures, hormone therapy when hormones were prepared from human donor sources, and prion contaminated instruments and devices. With regards to the latter, it is interesting to note that since 1960 there have only been six cases of CJD linked to medical instruments and devices, and all of these involved neurosurgical instruments or depth electrodes. Prion inactivation research conducted primarily in the UK has demonstrated that prions are highly resistant to inactivation using the cleaning and sterilization methods commonly used in hospitals. In 1999, the World Health Organization (WHO) convened a discussion to address adequate decontamination of prions in order to make neurosurgery and other CJD patient management

procedures safe. Several methods for decontaminating heat-stable medical instruments were recommended, and the most rigorous of these use a combination of strong chemicals such as sodium hydroxide or sodium hypochlorite and steam sterilization (autoclaving). When sodium hydroxide is selected, the instruments are immersed in this chemical and autoclaved. If the sodium hypochlorite method is chosen, the instruments are immersed in the chemical first, then rinsed thoroughly, and then subjected to autoclaving. The separation of the immersion step from the autoclave step in this instance prevents the hazardous generation of and exposure to chlorine gases. After the instruments are subjected to either of these decontamination protocols, they are then cleaned thoroughly and sterilized normally.

**What Are the Risks of CJD Transmission to Healthcare Workers and Linen Managers?**

Healthcare workers who have direct contact with prion-infected CNS tissues have the greatest potential risk for exposure. Neurosurgeons, pathologists, and histology technicians would be the healthcare professionals in this category. However, over the last 40 years, there have been only 24 cases of CJD diagnosed among healthcare workers, and the rates of infection in the occupations at risk are no higher than that in the general population. Animal studies have demonstrated that the "Chain of Infection" principles apply to the prevention and control of CJD.

Central to the infection control for this disease is to prevent infectious material (i.e., CNS tissue) from entering the correct portal of entry. In the cases involving contaminated medical instruments, prion contamination was introduced directly into the CNS of the surgical patient, which, in retrospect, was a highly efficient, albeit totally artificial, means of prion transmission. Transplant of contaminated dura mater from infected donors to the brains of recipients was also a very efficient method of transmission. All of these episodes are preventable, and efforts are underway to continue the assessment of donors, and to conduct a risk assessment of neurosurgical patients for possible CJD status prior to neurosurgery.

Care of the CJD patient elsewhere in the hospital requires no extraordinary care measures. Standard precautions are adequate for therapeutic and nursing procedures. According to Table 3, it's evident that blood, urine, sweat, and feces do not contain prions to any great extent. Consequently, the linens, towels, wash cloths, and gowns used during the care of the CJD patient do not become contaminated with prions under normal daily circumstances. These can be returned to the laundry for laundering as per normal procedures. Laundry workers should handle the linens and textiles from CJD patients' rooms with the same personal protective equipment (PPE) and procedures. There is no evidence that prions have been transmitted via aerosols in an airborne means of transmission. Nevertheless, the sensible approach to soiled laundry manipulation is that which minimizes the production of aerosols.

The only instance in which a different tactic may be considered is if the textile becomes contaminated with CNS tissue (such as during neurosurgery) or cerebrospinal fluid. Although there has been no evidence that CJD has been transmitted from textiles contaminated as such, it may be prudent to retrieve these textiles and send them for incineration. If CNS tissue or cerebrospinal fluid contaminates a hard surface, the spill area is decontaminated with 1 Normal (1N) sodium hydroxide for at least 30 minutes before cleaning up the spot as per guidelines from the Centers for Disease Control and Prevention (CDC).

**Summary**

In summary, CJD is a universally fatal disease, but at present it is considered a rare occurrence. While prions can be transmitted, they are not easily transmissible, as this occurs only under very limited circumstances. Healthcare workers, including those in hospital laundries and those providing linen/laundry services to healthcare facilities, are expected to have little or no risk of sustaining a bona fide occupational exposure to prions during the normal course of operations. Managers should expect that their workforce follow proper soiled linen handling procedures, use PPE as appropriate, and observe good linen management practices regardless of the medical status of the patients in the facility.

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