Creutzfeldt-Jakob Disease: Recommendations for Disinfection and Sterilization

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Prion diseases constitute a unique infection control problem because prions exhibit unusual resistance to conventional chemical and physical decontamination methods. Recommendations to prevent cross-transmission of infection from medical devices contaminated by Creutzfeldt-Jakob disease (CJD) have been based primarily on prion inactivation studies. The recommendations in this article consider inactivation data but also use epidemiological studies of prion transmission, infectivity of human tissues, and efficacy of removing microbes by cleaning. On the basis of the scientific data, only critical (e.g., surgical instruments) and semicritical devices contaminated with high-risk tissue (i.e., brain, spinal cord, and eye tissue) from high-risk patients—those with known or suspected infection with CJD—require special treatment.

Creutzfeldt-Jakob disease (CJD) is a degenerative neurological disorder of humans that affects ~1 person per million population per year both in the United States [1] and worldwide [2]. CJD is transmitted by a proteinaceous infectious agent, or “prion.” It has been estimated that the incubation period can vary from months to decades, but once symptoms develop, the disorder is usually fatal within 1 year. At present, there are no effective vaccines, no completely reliable and validated laboratory tests for detecting infection in presymptomatic people, and no specific therapy available for prion diseases.

CJD is classified as a transmissible spongiform encephalopathy (TSE) in humans; other TSEs in humans include kuru, Gerstmann-Straussler-Scheinker syndrome, and fatal familial insomnia syndrome (table 1). In recent years, a new variant form of CJD (vCJD) has been recognized. vCJD differs from CJD in many respects, including epidemiology, pathology, and geographic distribution (primarily in the United Kingdom). In addition to these 4 prion diseases in humans, 6 prion diseases in animals have been described: scrapie in sheep and goats, transmissible mink encephalopathy, exotic ungulate encephalopathy, chronic wasting disease of mule deer and elk, feline spongiform encephalopathy, and bovine spongiform encephalopathy (BSE, also known as “mad cow disease”). No prion disease elicits an immune response, and all such diseases result in a noninflammatory pathological process confined to the CNS [2].

CJD and other transmissible spongiform encephalopathies exhibit an unusual resistance to conventional chemical and physical decontamination methods [3]. Because CJD is not readily inactivated by conventional disinfection and sterilization procedures, and because of the invariably fatal outcome of CJD, the procedures for disinfection and sterilization of the CJD prion have been both conservative and controversial for many years. The purpose of this article is to critique the literature and develop evidence-based guidelines to prevent cross-transmission of infection from CJD-contaminated medical devices.

ETIOLOGY

Prions are a unique class of pathogens; an agent-specific nucleic acid (DNA or RNA) has not been detected. The infection is associated with the abnormal isoform of a host cellular protein called prion protein ("PrP") [2]. In humans, the PrP gene resides on chromosome 20; mutations in this gene may trigger the transformation of the PrP protein into the pathological isoform.
Table 1. Prion diseases in humans and their mode of transmission.

<table>
<thead>
<tr>
<th>Prion disease</th>
<th>Mechanism of pathogenesis</th>
<th>Incidence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creutzfeldt-Jakob disease</td>
<td>Germline mutations in PrP gene</td>
<td>1 per million</td>
</tr>
<tr>
<td>Familial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>Infection from prion-contaminated pituitary hormone, dura mater, etc.</td>
<td></td>
</tr>
<tr>
<td>Sporadic</td>
<td>Somatic mutation or spontaneous conversion of PrP(^\text{c}) to PrP(^\text{s})?</td>
<td></td>
</tr>
<tr>
<td>Variant</td>
<td>Infection from bovine prions?</td>
<td></td>
</tr>
<tr>
<td>Fatal familial insomnia</td>
<td>Germline mutations in PrP gene</td>
<td>&lt;1 per billion</td>
</tr>
<tr>
<td>Gerstmann-Straussler-Scheinker syndrome</td>
<td>Germline mutations in PrP gene</td>
<td>1 per billion</td>
</tr>
<tr>
<td>Kuru</td>
<td>Infection from ritualistic cannibalism</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^a\) Autosomal-dominant transmission; adapted from Johnson and Gibbs [2] and Prusiner [4].

This conversion of the normal cellular protein into the abnormal disease-causing isof orm (PrP\(^\text{c}\)) involves a conformational change whereby the \(\alpha\)-helical content diminishes and the amount of \(\beta\)-pleated sheet increases, resulting in profound changes in properties. For example, the PrP\(^\text{c}\) is susceptible to proteases and the PrP\(^\text{s}\) is partially resistant. No prion-specific nucleic acid is known to be required for transmission of disease [2, 4, 5]. The pathogenic prions accumulate in neural cells, disrupting function and leading to vacuolization and cell death. Korth et al. [6] have described a monoclonal antibody that distinguishes between the normal and disease form of PrP.

**EPIDEMIOLOGY OF CJD**

CJD is the most prevalent form of TSEs in humans (table 1). CJD is manifested clinically as a rapidly progressive dementia (cognitive imbalance) that includes psychiatric and behavioral abnormalities, coordination deficits, myoclonus, and a distinct triphasic and polyphasic electroencephalogram reading. Eighty percent of sporadic cases of CJD are diagnosed when the patient is aged 50–70 years. Definitive diagnosis of CJD requires a histological examination of the affected brain tissue [2, 4, 5].

CJD occurs as both a sporadic and familial disease. Approximately 10% of CJD cases are inherited and are caused by mutations in the PrP gene located on the short arm of chromosome 20. Less than 1% of CJD cases result from person-to-person transmission, primarily as a result of iatrogenic exposure. Approximately 90% of CJD cases are classified as sporadic because there is no family history and no known source of transmission. There is no seasonal distribution, no evidence of changing incidence rates, and no convincing geographic aggregation of cases [2, 4–7]. Ninety percent of the deaths in the United States are among people aged >55 years, and both sexes are affected equally. Death usually occurs within 6 months of appearance of symptoms (median age at death, 68 years) [1].

CJD is not transmitted by direct contact, or by droplet and airborne spread. Iatrogenic transmission of CJD from person to person has resulted from the direct inoculation, implantation, or transplantation of infectious materials either intracerebrally or peripherally. CJD can be transmitted from samples obtained from patients to nonhuman primates [2]. Transmission can occur by peripheral routes of inoculation, but peripheral routes require larger doses than does intracerebral inoculation. Oral transmission has been demonstrated with even larger doses [2, 8]. The incubation period depends on the dose of prions and the route of exposure. Studies have shown that prions (e.g., scrapie) are not inactivated by 3 years of environmental exposure [9].

**vCJD**

BSE was first identified in 1986 in the United Kingdom, and by November 2000, ~180,000 cattle had been infected [10]. BSE appeared to have resulted from the exposure of cattle to meat and bone meal that was produced by a new rendering process in which the temperature was reduced and the hydrocarbon solvent extraction step was omitted. The protein supplement was made from the remains of sheep and beef contaminated with scrapie and BSE [11]. In 1996, an advisory committee to the UK government announced its conclusion that the BSE agent might have spread to humans on the basis of the recognition of vCJD in 10 people during 1994–1995.

A total of 89 cases of vCJD in humans had been diagnosed (85 in the United Kingdom, 3 in France, and 1 in Ireland) by early November 2000 [10]. The epidemiological, clinical, and pathological profiles differ from those of sporadic CJD. The mean age at onset is 29 years (range, 16–48 years), compared with 65 years for sporadic CJD. The duration of illness is 14 months for vCJD and 4.5 months for sporadic CJD. Patients with vCJD frequently present with sensory and psychiatric symptoms that are uncommon in cases of sporadic CJD [5]. All patients with vCJD were potentially exposed to contaminated bovine animals during the 1980s, before measures to control human exposure were undertaken. Experimental evi...
idence that involved the intracerebral inoculation of cynomolgus macaque monkeys with brain tissue obtained from cattle with BSE supports a causal link between BSE and the vCJD; all monkeys developed a neuropathological phenotype similar to that described with vCJD but that differed from that of macaques inoculated with sporadic CJD [12]. vCJD has not been reported in the United States.

**INFECTIVITY OF TISSUE**

To date, all known cases of iatrogenic CJD have resulted from exposure to infectious brain, dura mater, pituitary, or eye tissue. This is likely due to the high levels of abnormal prions in the CNS. However, from the results of tissue infectivity studies in experimental animals and epidemiological studies in humans, it has been well established that the infectious agent may be present in many body tissues (table 2) but that prions are present in lower numbers than in the brain and, therefore, transmission is less likely. Consistent experimental transmission of infectivity has been possible with homogenates of brain, spinal cord, and eye tissue. Transmission occurs in less than half of the attempts with preparation of lung, liver, kidney, spleen, lymph node, and CSF. Transmission to primates has never been documented with any body fluid other than CSF [13, 14]. Prions have been isolated from the blood of infected guinea pigs, mice, and patients with CJD [15, 16]. There are no known cases of CJD attributable to the reuse of devices contaminated with blood or to the transfusion of blood products. Therefore, although transmission of CJD from human blood to laboratory animals by means of intracerebral inoculation have been reported [16], attempts to transmit CJD from CJD-infected patients to primates by means of whole blood or serum have failed [13].

**IATROGENIC CJD**

Iatrogenic CJD has been described in humans in 3 circumstances: after use of contaminated medical equipment (2 confirmed cases); after use of extracted pituitary hormones (>130 cases) or gonadotropin (4 cases); and after implantation of contaminated grafts from humans (cornea, 3 cases; dura mater, >110 cases) [3, 17]. Transmission by stereotactic electrodes is the only convincing example of transmission by means of a medical device. The electrodes had been implanted in a patient with known CJD disease and then cleaned with benzene and “sterilized” with 70% alcohol and formaldehyde vapor [18]. Two years later, these electrodes were retrieved and implanted into a chimpanzee in which the disease developed. The method used to “sterilize” these electrodes would not currently be considered an adequate method for sterilizing medical devices. The infrequent transmission of CJD by means of contaminated medical devices probably reflects the inefficiency of transmission (unless one is dealing with neural tissue) and the effectiveness of conventional cleaning and current disinfection and sterilization procedures. Retrospective studies suggest that 5 other cases may have resulted from the use of contaminated instruments in neurosurgical operations [17].

Johnson and Gibbs [2] reviewed the risks associated with blood products and concluded that CJD had not been transmitted by transfusion of human blood products. Evidence that supports this conclusion has included the following: case-control studies have not linked a history of transfusions to an increased risk of CJD [19]; the disease has not been reported in patients with hemophilia [20, 21]; injection drug use does not increase the risk [2]; investigation of recipients of blood components from known CJD donors has not revealed transmission of CJD [22]; and transfusion with full units of blood from patients with CJD to chimpanzees failed to induce CJD [23]. Although there have been no proven cases of CJD transmission by means of whole blood transfusions, these epidemiological studies could miss very rare events.

There is no evidence of occupational transmission of CJD to health care workers. Although cases of CJD have been reported in ~24 health care workers, this incidence does not exceed what would be expected by chance alone [5]. In the context of occupational exposure, the highest potential risk results from exposure to high-infectivity tissue through needlestick injuries with inoculation [3]. Exposure that results from splashing of the mucous membranes (notably, the conjunctiva) or unintentional ingestion may be considered a hypothetical risk [3]. For these reasons, all health care personnel who work with patients who have known or suspected prion diseases should use standard precautions.

### Table 2. Comparative frequency of risk of infection of organs, tissue, and body fluids of humans with transmissible spongiform encephalopathies.

<table>
<thead>
<tr>
<th>Risk of infection</th>
<th>Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>High&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Brain (including dura mater), spinal cord, and eye (e.g., cornneas)</td>
</tr>
<tr>
<td>Low&lt;sup&gt;b&lt;/sup&gt;</td>
<td>CSF, liver, lymph node, kidney, lung, and spleen</td>
</tr>
<tr>
<td>None&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Peripheral nerve, intestine, bone marrow, whole blood, leukocytes, serum, thyroid gland, adrenal gland, heart, skeletal muscle, adipose tissue, gingiva, prostate, testis, placenta, tears, nasal mucus, saliva, sputum, urine, feces, semen, vaginal secretions, and milk</td>
</tr>
</tbody>
</table>

**NOTE.** Adapted from Brown et al. [13] and Brown [14].

<sup>a</sup> Transmission to inoculated animals >50%.

<sup>b</sup> Transmission to inoculated animals >10%–20% (except for lung tissue, for which transmission is 50%), but no epidemiological evidence of human infection by means of these tissues.

<sup>c</sup> Transmission to inoculated animals is 0% (several tissues in this category had few tested specimens).
CONTROL MEASURES

We believe that infection control measures should be based on epidemiological evidence that links specific body tissues or fluids to transmission of CJD or on infectivity assays that demonstrate that body tissues or fluids are contaminated with infectious prions. The Centers for Disease Control and Prevention (CDC, Atlanta) [24, 25] has used these principles plus inactivation data to develop draft guidelines for reprocessing CJD-contaminated medical devices. Guidelines are also available from the World Health Organization (Geneva) [3] and from healthcare professionals [26, 27]. Other CJD recommendations primarily have been based on inactivation studies [27–29]. Our recommendations are also based on epidemiological data, infectivity data, cleaning data that use standard biological indicators, inactivation data for prions, risk of disease transmission associated with the use of the instrument or device, and review of other recommendations [3, 24–29] (see the Appendix).

Standard precautions should be used by healthcare workers when caring for patients with CJD. Use of added personal protective equipment, such as gowns or masks, is unnecessary in view of the lack of communicability of CJD to healthcare workers.

To minimize the possibility of use of neurosurgical instruments that have been potentially contaminated during procedures done on patients in whom CJD is later diagnosed, hospitals should consider using the sterilization guidelines outlined below for neurosurgical instruments used during brain biopsy done on patients in whom a specific lesion has not been demonstrated (e.g., by MRI and CT scans) [25]. Alternatively, neurosurgical instruments used in such cases could be disposable.

DISINFECTION AND STERILIZATION

Numerous studies on the inactivation of prions by germicides and sterilization processes have been conducted, but these studies do not reflect the reprocessing procedures in a clinical setting. First, these studies have not incorporated a cleaning procedure that normally reduces microbial contamination by 4 logs [29]. Second, the prion studies have been done with tissue homogenates, and the protective effect of tissue may explain, in part, why the TSE agents are difficult to inactivate [30]. Brain homogenates confer thermal stability to small subpopulations of the scrapie agent and some viruses. This subpopulation may be due to the protective effect of aggregation or population heterogeneity [30].

Favero [24] has explained that the draft guidelines of the CDC are based on a risk assessment that considers the cleaning and prion bioburden that results from contact with infectious tissues. Another component that must be integrated into the disinfection and sterilization process is the risk of infection.
Table 4. Chemicals demonstrated to be ineffective in the inactivation of prions (<3-log reduction in 1 h).

<table>
<thead>
<tr>
<th>Reference(s)</th>
<th>Agent</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>[31]</td>
<td>Phenol/phenolics</td>
<td>10% Lysol</td>
</tr>
<tr>
<td>[31]</td>
<td>Hydrogen peroxide</td>
<td>3%</td>
</tr>
<tr>
<td>[31]</td>
<td>Iodine</td>
<td>2%</td>
</tr>
<tr>
<td>[31, 32]</td>
<td>Chlorine dioxide</td>
<td>50 ppm</td>
</tr>
<tr>
<td>[31, 32, 43]</td>
<td>Formaldehyde</td>
<td>3.7%</td>
</tr>
<tr>
<td>[31–33, 36]</td>
<td>Potassium permanganate</td>
<td>0.1%–2%</td>
</tr>
<tr>
<td>[32]</td>
<td>Sodium deoxycholate</td>
<td>5%</td>
</tr>
<tr>
<td>[32]</td>
<td>Triton X-100</td>
<td>1%</td>
</tr>
<tr>
<td>[32, 33, 45]</td>
<td>Sodium dodecyl sulfate</td>
<td>0.5%–5%</td>
</tr>
<tr>
<td>[32, 39]</td>
<td>Glutaraldehyde</td>
<td>5%</td>
</tr>
<tr>
<td>[33]</td>
<td>Tego(dodecyl-di[aminoethyl]-glycine)</td>
<td>5%</td>
</tr>
<tr>
<td>[33]</td>
<td>Phenol/phenolics</td>
<td>0.6% Phenols</td>
</tr>
<tr>
<td>[36]</td>
<td>Ammonia</td>
<td>1.0 M</td>
</tr>
<tr>
<td>[36]</td>
<td>Urea</td>
<td>4–8 M</td>
</tr>
<tr>
<td>[36, 45]</td>
<td>Hydrochloric acid</td>
<td>1.0 N</td>
</tr>
<tr>
<td>[39]</td>
<td>Alcohol</td>
<td>100%</td>
</tr>
<tr>
<td>[39, 44]</td>
<td>Peracetic acid</td>
<td>19%</td>
</tr>
<tr>
<td>[42]</td>
<td>Alcohol</td>
<td>50%</td>
</tr>
</tbody>
</table>

associated with the use of the medical device. The 3 categories to which medical devices can be assigned are “critical,” “semicritical,” and “noncritical.” Items assigned to the critical category present a high risk of infection if they are contaminated with CJD as the device enters a sterile tissue or the vascular system. This category includes surgical instruments and implants. Semicritical items (e.g., endoscopes and respiratory therapy equipment) are devices that come into contact with mucous membranes or skin that is not intact. In general, these items should be free of all microorganisms, with the exception of small numbers of bacterial spores. Transmission of CJD by means of contact with mucous membranes or nonintact skin has not been described. Noncritical items (e.g., floors, walls, blood pressure cuffs, and furniture) come into contact with intact skin but not with mucous membranes. Intact skin should act as an effective barrier to microorganisms and prions. Therefore, a critical or semicritical device that has contact with high-risk tissue (e.g., brain) from a high-risk patient (e.g., with suspected or known CJD) must be reprocessed in a manner to ensure the elimination of prions. The combined contribution of cleaning and use of an effective physical or chemical reprocessing procedure should eliminate the risk of CJD transmission. Critical or semicritical instruments or medical devices that have contact with low-risk or no-risk tissue can be treated by means of conventional methods, because the devices have not resulted in transmission of CJD (see the Appendix).

To assess the effectiveness of disinfection or sterilization procedures, one must consider the inactivation and removal factor [31–33]—that is, the reduction of infectious units during the disinfection or sterilization process. Therefore, the probability of an instrument remaining capable of transmitting disease depends on the initial degree of contamination and the effectiveness of the decontamination procedures. An instrument contaminated with 50 mg of brain tissue from a person infected with CJD and with a titer of $1 \times 10^5$ (50% lethal dose intracerebral units/g) [13] would have $5 \times 10^3$ infectious units. It has been suggested that a titer loss of $10^4$ prions should be regarded as an indication of appropriate disinfection of CJD [33]. However, the effectiveness of a disinfection or sterilization procedure should be considered in conjunction with the effectiveness of cleaning. Studies done with microbial agents demonstrate that cleaning done according to conventional methods used in health care results in a reduction of $10^6$ microbes. Therefore, cleaning followed by disinfection would result in a titer loss of $10^5$ (4-log reduction with cleaning plus >3-log reduction with an effective disinfection process), whereas tissues with high prion infectivity (e.g., brain) would be contaminated with $10^5$ prions/g. Cleaning, followed by use of a disinfection or sterilization procedure should destroy infectivity and provide a significant safety margin.

Disinfection. Results of chemical inactivation studies of prions have been inconsistent because of the use of differing methodologies, including the following: strain of prion (e.g., prions may vary in thermostability, but differential susceptibility to disinfectants has not been described), prion concentration in brain tissue, test tissues (e.g., intact brain tissue, brain homogenates, and partially purified preparations), test animals, duration of follow-up of inoculated test animals, exposure container, log decrease calculated from incubation period assays rather than from end-point titrations, concentration of a disinfectant (e.g., chlorine) at the beginning and end of an experiment, exposure conditions, and cycle parameters of the sterilizer [27]. Despite these limitations, there is some consistency in the results. An important limitation of current research on disinfection is that, currently, prion assays are slow, laborious, and costly. Studies that evaluate the efficacy of a combination of cleaning and disinfection have not been published.

It has been established that most disinfectants are inadequate for the elimination of prion infectivity. There are 4 chemicals that reduce a titer by >4 logs: chlorine, a phenolic, guanidine thiocyanate, and sodium hydroxide (table 3) [31–39]. Of these 4 chemical compounds, the disinfectant that is available and that provides the most consistent prion inactivation results is chlorine, but even chlorine has had unexplainable reduced activity (e.g., reduction of 3.3 logs of CJD in 60 min by use of 2.5% hypochlorite) [36]. The corrosive nature of chlorine would make it unsuitable for semicritical devices such as endoscopes. Several investigators have found that CJD is completely inactivated by 1 N NaOH [35, 40, 41]. Other anti-
microbial agents that have been shown to be ineffective (<3 log reduction in 1 h) against CJD or other TSEs are listed in table 4 [31–33, 36, 39, 42–45]. Studies have also shown that aldehydes, such as formaldehyde, enhance the resistance of prions and that pretreatment of scrapie-infected brain tissue with formaldehyde abolished the inactivating effect of autoclaving [46]. A formalin–formic acid procedure is required for inactivation of prion infectivity in tissue samples obtained from patients with CJD [47].

Both flexible and rigid endoscopes have been used in neurosurgery [48, 49]. If such scopes come into contact with high-risk tissue in a patient with known or suspected CJD, either the scopes should undergo sterilization (if possible), or single-use devices should be used. Endoscopes that come into contact with other tissues (e.g., from the gastrointestinal tract, respiratory tract, joints, and abdomen) can be disinfected by conventional methods.

**Sterilization.** Prions exhibit an unusual resistance to conventional chemical and physical decontamination methods. These include both gaseous (e.g., ethylene oxide and formaldehyde) and physical processes (e.g., dry heat, glass bead sterilization, boiling, and autoclaving at conventional exposure conditions [at 121°C for 15 min]) [27, 32, 36, 39]. Rohwer’s [30] data suggest that the majority of scrapie infectivity is inactivated by brief exposure to temperatures of ≥100°C. For example, when scrapie strain 263K was exposed to a temperature of 121°C, 99.9999% of the infectivity was destroyed during the minute of exposure required to bring the sample to temperature. At 100°C, 97% was destroyed within 2 min of exposure at temperature. Therefore, only a fraction of the infectious activity is extremely resistant.

Standard gravity displacement steam sterilization at 121°C has been studied with different strains of CJD, BSE, and scrapie and has been shown to be only partially effective, even after exposure times of 120 min. As the temperature and exposure time was increased, greater inactivation of the prion agents was achieved (table 5). Although there is some disagreement about the ideal time and temperature cycle [26], the recommendations of 121°C–132°C for 60 min (gravity) and of 134°C for ≥18 min (prevacuum) are reasonable on the basis of the scientific literature. These methods should result in a decrease of >5 logs, and cleaning should result in a 4-log reduction, which provides a significant margin of safety (brain tissue concentration 10⁷ prions/g) [13]. Other steam sterilization cycles, such as 132°C for 15 min (gravity), have been shown to be only partially effective [36].

Several investigators have found that combining sodium hydroxide (0.09 N for 2 h) with steam sterilization at 121°C for 1 h results in complete inactivation of infectivity (>7.4 logs) [38]. However, the combination of sodium hydroxide and steam sterilization may be deleterious to surgical instruments [27].

### Table 5. Effectiveness of high temperature sterilization (with and without pretreatment with NaOH) against prions.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Temperature</th>
<th>Prion concentrationa</th>
<th>Agent (strain)</th>
<th>Animal</th>
<th>Log decrease, LD&lt;sub&gt;50&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>[33]</td>
<td>136°C (porous)</td>
<td>7.4</td>
<td>Scrapie (139A)</td>
<td>Mice</td>
<td>≥6.9 at 4, 8, 16, and 32 min</td>
</tr>
<tr>
<td>[33]</td>
<td>136°C (porous)</td>
<td>6.1</td>
<td>Scrapie (22A)</td>
<td>Mice</td>
<td>≥5.6 at 4, 8, 16, and 32 min</td>
</tr>
<tr>
<td>[33]</td>
<td>126°C (gravity)</td>
<td>7.4</td>
<td>Scrapie (139A)</td>
<td>Mice</td>
<td>5.9 at 15 min and at 30 min, ≥6.9 at 1 h and at 2 h</td>
</tr>
<tr>
<td>[33]</td>
<td>126°C (gravity)</td>
<td>6.1</td>
<td>Scrapie (22A)</td>
<td>Mice</td>
<td>1.8 at 15 min, 2.1 at 30 min, 3.6 at 1 h, 2.9 at 2 h</td>
</tr>
<tr>
<td>[34]</td>
<td>121°C (gravity)</td>
<td>5.8</td>
<td>CJD (Kitasato-1)</td>
<td>Mice</td>
<td>3.1 at 30 min, 3.8 at 1 h, 4.2 at 2 h</td>
</tr>
<tr>
<td>[34]</td>
<td>1 N NaOH for 1 h plus 121°C for 30 min</td>
<td>5.8</td>
<td>CJD (Kitasato-1)</td>
<td>Mice</td>
<td>≥4</td>
</tr>
<tr>
<td>[34]</td>
<td>132°C (gravity)</td>
<td>5.8</td>
<td>CJD (Kitasato-1)</td>
<td>Mice</td>
<td>&gt;4.8 at 30 min and at 1 h</td>
</tr>
<tr>
<td>[35]</td>
<td>134°C (porous)</td>
<td>9.3</td>
<td>Scrapie (263K)</td>
<td>Hamsters</td>
<td>7.2 at 18 min</td>
</tr>
<tr>
<td>[35]</td>
<td>134°C–138°C (porous)</td>
<td>3.6</td>
<td>BSE</td>
<td>Mice</td>
<td>2.5 at 18 min</td>
</tr>
<tr>
<td>[36]</td>
<td>132°C</td>
<td>6.1–7.2</td>
<td>CJD (S.Co.)</td>
<td>Guinea pigs</td>
<td>≥5 at 1 h</td>
</tr>
<tr>
<td>[36]</td>
<td>121°C</td>
<td>6.1–7.2</td>
<td>CJD (S.Co.)</td>
<td>Guinea pigs</td>
<td>≥5 at 1 h</td>
</tr>
<tr>
<td>[38]</td>
<td>0.09 N or 0.9 N NaOH for 2 h plus 121°C (gravity) for 1 h</td>
<td>7.4</td>
<td>Scrapie (263K)</td>
<td>Hamsters</td>
<td>≥7.4</td>
</tr>
<tr>
<td>[38]</td>
<td>121°C (gravity)</td>
<td>7.4</td>
<td>Scrapie (263K)</td>
<td>Hamsters</td>
<td>≥5 at 1 h and at 1.5 h</td>
</tr>
<tr>
<td>[38]</td>
<td>132°C (gravity)</td>
<td>7.4</td>
<td>Scrapie (263K)</td>
<td>Hamsters</td>
<td>≥6 at 1 h, 7.4 at 1.5 h</td>
</tr>
</tbody>
</table>

**NOTE.** All experiments used brain homogenates or brain macerates, and no experiment cleaned the inoculum. BSE, bovine spongiform encephalopathy; CJD, Creutzfeldt-Jakob disease; LD<sub>50</sub>, 50% lethal dose.

a 50% Lethal dose intracerebral log units/g.
CONCLUSION

Prion diseases are rare and thus do not constitute a major infection control risk. Nevertheless, prions represent an exception to conventional disinfection and sterilization practices. These guidelines for CJD disinfection and sterilization are based on consideration of epidemiological data, infectivity data, and cleaning and inactivation studies. Guidelines for the management of both patients infected with CJD and equipment should be modified as additional scientific information (e.g., transmissibility of variant CJD, efficacy of cleaning instruments contaminated with prions) becomes available. A task force that represents professional organizations and researchers could develop a consensus guideline for the United States that represents the optimal and practical conditions for inactivation of CJD. The CDC's draft guideline and other evidence-based recommendations could serve as models for this consensus statement. Finally, studies consistent with actual clinical practices (e.g., surgery performed on infected animals and then followed by cleaning of instruments with enzymatic detergents and disinfection or sterilization) should be undertaken.

APPENDIX

INFECTION CONTROL PRECAUTIONS FOR PATIENTS WITH KNOWN OR SUSPECTED CJD

General Precautions

1. Precautions are used for all patients with known or suspected prion disease and for those at high risk for the development of a prion disease, including all patients with rapidly progressive dementia; those with possible Creutzfeldt-Jakob disease (CJD), Gerstmann-Straussler-Scheinker syndrome (GSS), fatal familial insomnia (FFI), or variant Creutzfeldt-Jakob disease (vCJD); and those who have received dura mater transplants or human growth hormone injection.

2. Standard precautions should be used for all patients with known or suspected CJD. Additional precautions (e.g., contact) are not necessary. Gloves should be worn for the handling of blood and body fluids (e.g., secretions and excretions). Masks, gowns, and protective eyewear should be worn if exposure to blood or other material that is potentially infectious to mucous membranes or skin is anticipated.

3. Because standard decontamination of tissue samples (e.g., formalin) or specimens may not inactivate CJD, all tissue samples should be handled using standard precautions (i.e., gloves). The tissue samples and specimens should be labeled as a "biohazard" and as "suspected CJD" before being sent to the laboratory.

4. No special precautions are required for disposal of body fluids. Such fluids may be disposed of by means of a sanitary sewer. Blood or blood-contaminated fluids should be managed per state regulations for regulated medical waste.

5. Regulated medical waste (e.g., bulk blood, pathological waste, microbiological waste, and sharps) should be managed per state regulations.

6. Laundry should be managed as required by the Occupational Safety and Health Administration (OSHA) rule on bloodborne pathogens. No additional precautions are required.

7. No special precautions are required for the handling of food utensils.

8. When a patient dies, ensure that the morgue and funeral home are notified that the patient has CJD. No excess precautions need to be taken with regard to burial (e.g., no special cemetery is required).

9. Patients with known or suspected prion disease should not serve as donors for organs, tissues, blood components, or sources of tissue (e.g., dura mater and hormones).

10. Infection control professionals and other departments involved with infection control (e.g., surgical services, central processing, and pathology) should be notified by clinicians when a patient with a known or suspected prion disease is scheduled to undergo any invasive procedure in which there may be exposure of personnel or instruments that contain potentially infectious tissues.

11. Clinicians should notify infection control professionals of all patients with a known or suspected prion disease.

Decontamination of Contaminated Medical Devices

High-risk tissues (defined as brain [including dura mater], spinal cord, and eyes) from high-risk patients (e.g., those with known or suspected CJD) and critical or semicritical items:

1. Those devices that are constructed so that cleaning procedures result in effective tissue removal (e.g., surgical instruments) can be cleaned and then sterilized by autoclaving either at 134°C for ≥18 min in a prevacuum sterilizer or at 121°C–132°C for 1 h in a gravity displacement sterilizer.

2. Those devices that are impossible or difficult to clean could be discarded. Alternatively, one should place the contaminated items in a container filled with a liquid (e.g., saline, water, or phenolic solution) to retard adherence of material to the medical device. This should be followed by initial decontamination done by autoclaving at 134°C for 18 min in a prevacuum sterilizer (liquids must be removed before sterilization) or at 121°C–132°C for 1 h in a gravity displacement sterilizer, or by soaking in 1 N NaOH for 1 h. Finally, terminal cleaning, wrapping, and sterilization can be done by conventional means.

3. To minimize drying of tissues and body fluids on the object,
instruments should be kept moist until cleaned and decontaminated.
4. Flash sterilization should not be used for reprocessing.
5. Items that permit only low-temperature sterilization (e.g., ethylene oxide or hydrogen peroxide gas plasma) should be discarded.
6. Contaminated items that are not processed according to these recommendations (e.g., medical devices used for brain biopsy before diagnosis) should be recalled and appropriately reprocessed. To minimize patient exposure to neurosurgical instruments from a patient who is later given a diagnosis of CJD, hospitals should consider using the aforementioned sterilization guidelines for neurosurgical instruments used on patients undergoing brain biopsy when a specific lesion has not been demonstrated. Alternatively, neurosurgical instruments used in such cases could be disposable.
7. Environmental surfaces (noncritical) contaminated with high-risk tissues (e.g., laboratory surface in contact with brain tissue of a person infected with CJD) should be cleaned and then spot-decontaminated with a 1:10 dilution of sodium hypochlorite (i.e., bleach). To minimize environmental contamination, disposable cover sheets could be used on work surfaces.
8. Noncritical equipment contaminated with high-risk tissue should be cleaned and then disinfected with a 1:10 dilution of sodium hypochlorite or 1 N NaOH, depending on material compatibility. All contaminated surfaces must be exposed to the disinfectant.
9. Equipment that requires special prion reprocessing should be tagged after use. Clinicians and reprocessing technicians should be thoroughly trained on how to properly tag the equipment and the special prion reprocessing protocols.
10. For ease of cleaning and to minimize percutaneous injury and generation of aerosols, use nonpowered instruments (e.g., drills or saws) or ensure that disposable protective equipment covers are available for powered instruments.

**Low-risk tissues** (defined as the CSF, kidney, liver, spleen, lung, and lymph nodes) from a high-risk patient and a critical or semicritical medical device:

1. These devices can be cleaned and either disinfected or sterilized by use of conventional protocols of heat or chemical sterilization, or by means of high-level disinfection.
2. Environmental surfaces contaminated with low-risk tissues or fluids require only standard disinfection (use disinfectants recommended by OSHA for decontamination of blood-contaminated surfaces [e.g., 1:10 to 1:100 dilution of 5.25% sodium hypochlorite]). To minimize environmental contamination, disposable cover sheets could be used on work surfaces.

**Occupational exposure:**

1. Care must be taken to avoid self-inoculation with sharp objects.
2. Although scientifically unproven, percutaneous exposure to the CSF or brain tissue of an infected person may be followed by rinsing the wound with 0.5% sodium hypochlorite (or 1 N of sodium hydroxide) for several minutes and then washing with soap and water.
3. Mucous membrane exposure to infectious tissues or fluids should be managed by irrigating the mucous membranes thoroughly with saline for several minutes.

**References**


