SHEA GUIDELINE

Guideline for Disinfection and Sterilization of Prion-Contaminated Medical Instruments

William A. Rutala, PhD, MPH; David J. Weber, MD, MPH

EPIDEMIOLOGY OF THE CREUTZFELDT-JAKOB DISEASE PRION

Creutzfeldt-Jakob disease (CJD) is a degenerative neurologic disorder of humans with an incidence in the United States of approximately 1 case per million population per year.[1-3] CJD is caused by a proteinaceous infectious agent, or prion. CJD is related to other human transmissible spongiform encephalopathies (TSEs), including kuru (US incidence, 0 [now eradicated]), Gerstmann-Straüssler-Scheinker syndrome (US incidence, 1 case per 40 million population per year), and fatal familial insomnia syndrome (incidence, <1 case per 40 million population per year). Prion diseases elicit no immune response, result in a noninflammatory pathologic process confined to the central nervous system, have an incubation period of years, and usually are fatal within 1 year after diagnosis.

A variant form of CJD (vCJD) has been recognized that is acquired from cattle with bovine spongiform encephalopathy (or "mad cow disease"). As of July 2009, a total of 211 cases of vCJD have been reported worldwide: 165 in the United Kingdom, 25 in France, 5 in Spain, 4 in Ireland, 3 each in the United States and the Netherlands, 2 in Portugal, and 1 each in Italy, Canada, Japan, and Saudi Arabia.[4-6] Two of the patients from Ireland, 2 patients from the United States, and 1 patient each from Canada, France, and Japan are believed to have been exposed to bovine spongiform encephalopathy during their past residence in the United Kingdom; the third US patient likely acquired vCJD in Saudia Arabia. Patients with vCJD are younger than patients with CJD (median age at death, 28 vs 68 years), have a longer duration of illness (14 months vs <6 months), and usually present with psychiatric or sensory symptoms that are uncommon with CJD. The association of vCJD with bovine spongiform encephalopathy is the first instance of apparent transmission of a TSE across the species barrier to humans. Chronic wasting disease of deer and elk was recognized in the United States more than 20 years ago. It has been identified in several states, beyond its original area of occurrence in the Rocky Mountains. To date, no evidence for transmission of chronic wasting disease of deer and elk to humans has been identified.[7-10]

TRANSMISSION OF CJD VIA MEDICAL DEVICES

CJD occurs as both a sporadic disease (~85% of cases) and as a familial or inherited disease (~15% of cases). Fewer than 1% of cases of CJD have resulted from healthcare-associated transmission; the majority of these result from the use of contaminated tissues or grafts.[11] Iatrogenic CJD has been described in humans in 3 circumstances: in patients for whom contaminated medical equipment was used during intracranial placement of contaminated electroencephalography electrodes (2 cases in Switzerland) or neurosurgical procedures (4 suspected cases: 3 cases in the United Kingdom and 1 case in France), in patients who received hormone therapy with cadaveric human growth hormone or gonadotropin (>190 cases [26 cases in the United States]; since 1985, human growth hormone has been manufactured by the use of recombinant DNA technology, which eliminated this risk), and in patients who received an implant of contaminated grafts from humans (cornea, 2 cases; dura mater, >190 cases [3 cases in the United States for which the risk factor is the Lyodura graft {B. Braun Melsungen} processed before 1987]).[11-14] All known instances of iatrogenic CJD have resulted from exposure to infectious brain, pituitary, or eye tissue. Tissue infectivity studies in experimental animals have determined the infectiousness of different body tissues (Table 1).[14,15]

Transmission to 2 patients via stereotactic electrodes is the only proven example of transmission by way of a medical device. The electrodes had been implanted in a patient with known CJD and then cleaned with benzene and "sterilized" with 70% alcohol and formaldehyde vapor produced by a formaldehyde generator using solid paraformaldehyde. Two years after the transmission to the 2 patients, these electrodes were retrieved and implanted into the brain of a chimpanzee, which subsequently developed the disease.[21] The method used

From Hospital Epidemiology, University of North Carolina Health Care (both authors), and the Division of Infectious Diseases, University of North Carolina School of Medicine (both authors), Chapel Hill, North Carolina.

Received November 9, 2009; accepted November 19, 2009; electronically published January 6, 2010.

© 2010 by The Society for Healthcare Epidemiology of America. All rights reserved. 0899-823X/2010/3102-0001$15.00. DOI: 10.1086/650197

TABLE 1. Comparative Frequency of Infectivity in Organs, Tissue, and Body Fluids of Humans with Transmissible Spongiform Encephalopathies (Creutzfeldt-Jakob Disease)

Infectious risk[a]	Tissue
High	Brain (including dura mater), spinal cord, posterior eye, pituitary tissue
Low	Cerebrospinal fluid, liver, lymph node, kidney, lung, spleen, placenta, olfactory epithelium
No risk	Peripheral nerve, intestine, bone marrow, whole blood, leukocytes, serum, thyroid gland, adrenal gland, heart, skeletal muscle, adipose tissue, gingiva, prostate, testis, tears, saliva, sputum, urine, feces, semen, vaginal secretions, milk, sweat

NOTE. Modified from Brown[14] and Brown et al,[15] with information from other studies.[16-20]

[a] High risk indicates a rate of transmission to inoculated animals of >50%; low risk indicates a rate of transmission to inoculated animals of ⩾10%–20% (except for lung tissue, for which transmission is 50%); no risk indicates a rate of transmission to inoculated animals of 0% (several tissues in this category had few tested specimens).

to "sterilize" these electrodes would not now be considered an adequate method for sterilizing medical devices. The fact that no known cases of CJD transmitted by way of contaminated medical devices have occurred in the past several decades probably reflects the inefficiency of transmission unless neural tissue is involved, and the effectiveness of conventional cleaning and current disinfection and sterilization procedures, although suboptimal, may be adequate to prevent disease transmission.[11,16] Retrospective studies suggest that 4 other cases of CJD may have resulted from the use of contaminated instruments in neurosurgical operations.[14,22,23] In one case the surgical instruments were cleaned with soap and water and then exposed to dry heat for an unspecified time at an unspecified temperature.[23] All 6 cases of CJD associated with neurosurgical instruments occurred in Europe during the period from 1952 through 1976, and details of the methods used to reprocess the instruments are incomplete.[11] Case-control studies have been performed to evaluate whether a proportion of sporadic cases of CJD result from covert, low-level contamination events during surgical procedures, and these studies have provided conflicting results.[24] In a series of cases, no secondary iatrogenic cases could be attributed to reuse of ophthalmic surgical instruments.[25] There are no known cases of sporadic CJD attributable to the reuse of devices contaminated with blood or to the transfusion of blood products.[26]

INACTIVATION OF THE CJD PRION

The prions that cause CJD and other TSEs exhibit an unusual resistance to conventional chemical and physical decontamination methods. Because the CJD agent is not readily inactivated by means of 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 cautious and controversial for many years.

The inactivation of prions by means of disinfection and sterilization processes has been studied by several investigators (Tables 2 and 3), but, until recently, these studies have not reflected the reprocessing procedures used in a clinical setting. First, these studies have not incorporated a cleaning procedure employing alkaline or enzymatic detergents, which normally reduces microbial contamination by a factor[53,54] of 4–6 $\log_{10}$ and reduces protein contamination.[55-58] While prions have been shown to bind tightly to surfaces and to be difficult to remove by cleaning,[59] there are now numerous studies that have shown the effectiveness of specific formulations of alkaline and enzymatic detergents to eliminate the infectivity of prions.[27-32,60-67] Caution must be exercised in the use of enzymatic detergents with prion-contaminated instruments, since some enzymatic detergents have been shown to be prionicidal while others have been shown to increase resistance to subsequent inactivation by steam sterilization.[29,33]

Second, the prion studies have been performed with tissue homogenates, and the protective effect of tissue may explain, in part, why the CJD agent is difficult to inactivate.[68] When testing the efficacy of autoclaving, some investigators employed procedures such as using "lumps" of prion-infected tissue of 50 or 375 mg; they found that the larger tissue samples were more refractory to inactivation.[69] Brain homogenates have been shown to confer thermal stability to small subpopulations of the scrapie agent and some viruses.[68] However, surgical instruments that had been processed in the central processing departments of 5 hospitals were shown to have a median protein contamination level of 8–91 μg per instrument.[70] Given a scenario in which there is 100 μg of protein on an instrument and given that brain tissue from a person infected with CJD has a titer of 10^5 (mean infectivity calculated from a total group of 27; 50% lethal dose intracerebral units per gram),[15] the instrument would have 10 potentially infectious units, without considering the prionicidal activity of the reprocessing steps. Clearly, special prion reprocessing measures discussed in this guideline will eliminate the prion infectivity with a substantial margin of safety. This small number of infectious units is unlikely to be a hazard even with standard instrument reprocessing. However, on the basis of current knowledge, special prion reprocessing should be used to provide the greatest margin of safety.

Third, results of inactivation studies of prions have been variable because of the use of differing methods, which may have varied according to prion strain (eg, the differing thermostability of TSEs such as scrapie prion strain 263K or 22A

TABLE 2. Efficacy of Sterilization Processes in Inactivating Prions

Ineffective ($\leqslant 3$ $\log_{10}$ reduction within 1 hour)	Effective (>3 $\log_{10}$ reduction from 18 minutes to 3 hours)
Autoclave at standard exposure conditions (121°C for 15 minutes)	Autoclave at 121°C–132°C for 1 hour (gravity displacement sterilizer) or 121°C for 30 minutes (prevacuum sterilizer)
Boiling	Autoclave at 134°C for 18 minutes (prevacuum sterilizer)
Dry heat	Autoclave at 134°C for 18 minutes immersed in water
Ethylene oxide	Hydrogen peroxide gas plasma (Sterrad NX)
Formaldehyde	Radiofrequency gas plasma
Hydrogen peroxide gas plasma, Sterrad 100S (ASP)	Sodium dodecyl sulfate, 2%, plus acetic acid, 1%, plus autoclave at 121°C for 15–30 minutes
Ionizing radiation	Sodium hydroxide (NaOH), 0.09 N or 0.9 N, for 2 hours plus autoclave at 121°C for 1 hour (gravity displacement sterilizer)
Microwave	Vaporized hydrogen peroxide, 1.5–2 mg/L
UV light	

NOTE. The same process may be listed as both effective and ineffective because of differences in sterilant concentration, exposure time, temperature, etc, or differences in testing methods. All of these experiments were performed without cleaning. Modified from Rutala and Weber,[16] with information from other studies.[27-52]

or ME7, bovine spongiform encephalopathy prion strain 6PB1 or 301V, vCJD prion, and sporadic CJD prion), prion concentration, prion detection,[34] tissue or composition of the brain material tested (intact brain tissue, brain homogenates, or partially purified preparations), animals tested, surfaces tested (eg, plastic or stainless steel), testing method (in vivo or vitro [eg, Western blot]), duration of follow-up of inoculated animals, exposure container (eg, open or closed), method of calculating $\log_{10}$ reductions in infectivity, concentration of the disinfectant at the beginning and end of the experiment, cycle parameters of the sterilizer, type of sterilizer (eg, gravity vs vacuum or porous steam sterilizers), and exposure conditions. Methodological issues have been found to significantly affect the antimicrobial testing results for all pathogens[71-76] and likely explain the varying results seen with various chemical disinfection methods (eg, use of sodium hydroxide [NaOH] or chlorine) and sterilization methods (eg, steam sterilization at 134°C for 18 minutes vs exposure to NaOH plus steam sterilization). Despite these limitations, there is a consistent pattern in the results.[16,77]

On the basis of the disinfection studies, many, but not all, disinfection processes fail to inactivate clinically important numbers of prions (Table 3).[16,27-31,33-52] There are several chemicals that reduce the prion titer by >3 $\log_{10}$ in 1 hour, but few of them have been used as disinfectants in healthcare facilities (Table 3). Of these chemical compounds, chlorine and NaOH have provided the most consistent prion inactivation results.[16] However, both NaOH and chlorine are corrosive and unsuitable for semicritical devices, such as endoscopes.

Several recent studies have demonstrated that prions are inactivated by cleaners such as alkaline detergents and enzymatic detergents.[17,27-30,32,40,48,60-67] Many of these studies used surgical stainless steel wires that were experimentally contaminated with prions; the contaminated wires efficiently transmitted the prion disease after implantation in the brains of mice or hamsters.[28,29,32,33,36,49,78] Several reports have demonstrated the possibility that available decontamination procedures using alkaline or enzymatic detergents (eg, Klenzyme [Steris], Hamo-100 [Steris], Septo-Clean [Septo-Clean], CIP100 [Steris], Prionzyme-M [Genencor], or Rely-On [DuPont])[40,48] could significantly reduce the infectivity of TSE agents (eg, scrapie prion strain 263K) and thus minimize or prevent the risk of iatrogenic transmission of undiagnosed or misdiagnosed CJD.[17,27,28,36,40,48,60,63,64,66,79,80] Other studies have revealed that specific phenolic compositions[27,28,81,82] or sodium dodecyl sulfate plus acetic acid may prove to be potent reagents for inactivation of prions.[37,79] It seems clear that the use of specific formulations of alkaline or enzymatic detergents in combination with standard sterilization processes could lead to the development of a validated method for the sterilization of prion-contaminated medical devices.[17,29,30,37,40,60,64,80]

Prions also exhibit an unusual resistance to conventional physical decontamination methods (Table 2).[16,27-52] While there is some disagreement on the ideal time and temperature cycle for autoclaving, the recommendation of 134°C for at least 18 minutes (prevacuum) or 132°C for 60 minutes (gravity displacement) is based on the scientific literature.[29-33,41,43-45,47,51,52,89,83] Some investigators have also found that combining sodium hydroxide (eg, 0.09N or 0.9N for 2 hours) with steam sterilization for 1 hour at 121°C results in partial or complete loss of infectivity.[29,41,47] However, the combination of exposure to NaOH and steam sterilization may be deleterious to surgical instruments[77,90] and sterilizers (T. K. Moore, written communication, October 2002), as well as to sterilizer operators, who could be breathing vaporized chemicals unless engineering controls or use of personal protective equipment prevents exposure. This risk can be minimized by the use of polypropylene containment pans and lids designed so that condensation collects and drips back into the pan.[90] Hot NaOH (250°F) is more caustic than NaOH at room temperature, so even greater care should be taken to avoid exposure to it (D. Asher, written communication, November 2002).

Until recently, low-temperature sterilization technologies (eg, use of ethylene oxide) have not demonstrated their

TABLE 3. Efficacy of Chemicals in Inactivating Prions

Ineffective ($\leq$3 $\log_{10}$ reduction within 1 hour)	Effective (>3 $\log_{10}$ reduction within 1 hour at temperatures of 20°C–55°C)
Acetone	Alkaline detergent (specific formulations)
Alcohol, 50%–100%	Chlorine, >1,000 ppm
Alkaline detergent (specific formulations)	Copper, 0.5 mmol/L, and hydrogen peroxide, 100 mmol/L
Ammonia, 1.0 M	Enzymatic detergent (specific formulations)
Chlorine dioxide, 50 ppm	Guanidine thiocyanate, >3 M
Enzymatic detergent (specific formulations)	Hydrogen peroxide, 59%
Formaldehyde, 3.7%	Peracetic acid, 0.2%
Glutaraldehyde, 5%	Phenolic disinfectant (specific formulation), >0.9%
Hydrochloric acid, 1.0 N	Quaternary ammonium compound (specific formulation)
Hydrogen peroxide, 0.2%, 3%, 6%, 30%, 60%	Sodium dodecyl sulfate, 2%, and acetic acid, 1%
Iodine, 2%	Sodium hydroxide, $\geq$1 N
Ortho-phthalaldehyde, 0.55%	Sodium metaperiodate, 0.01 M
Peracetic acid, 0.2%–19%	
Phenol/phenolics (concentration variable)	
Potassium permanganate, 0.1%–0.8%	
Quaternary ammonium compound (specific formulation)	
Sodium dodecyl sulfate, 1%–5%	
Sodium deoxycholate 5%	
Tego (dodecyl-di[aminoethyl]-glycine), 5%	
Triton X-100, 1%	
Urea, 4–8 M	

NOTE. The same process may be listed as both effective and ineffective because of differences in chemical concentration, exposure time, temperature, pH, etc, or differences in testing methods. All of these experiments were done without cleaning. Modified from Rutala and Weber,[16] with information from other studies.[27-30,32-35,37-39,42,44-49,60,61,64,66,78-88]

effectiveness at inactivating prions (Table 2) and have not been used to sterilize prion-contaminated medical instruments. Several peer-reviewed studies have revealed that newer low-temperature sterilization technologies (ie, hydrogen peroxide gas plasma used in the Sterrad NX [ASP] and vaporized hydrogen peroxide) can eliminate the infectivity of prions on stainless steel wires and may be useful for reducing (or preventing) risk associated with prion-contaminated devices.[29,32,33,36] These technologies, combined with use of prionicidal detergents, should sterilize prion-contaminated heat-sensitive medical devices, but a recommendation for using these technologies will be withheld until corroborative studies are published.[27,32,33,36]

DECONTAMINATION, DISINFECTION, AND STERILIZATION OF PRION-CONTAMINATED MEDICAL DEVICES

For a surgical instrument to act as a vehicle of prion transmission, it must come into contact with infective tissue (eg, brain) during surgery of the infected patient, it must retain the infectivity of any adhered matter after being decontaminated and sterilized, and it must have contact with the receptive tissue in the recipient.[91] The disinfection and sterilization recommendations for CJD in this guideline should break this chain of events and are based on the belief that infection prevention measures should be predicated on epidemiologic evidence linking specific body tissues or fluids to transmission of CJD; infectivity assays that demonstrate that body tissues or fluids are contaminated with infectious prions; cleaning data based on the use of detergents, microbiological indicators, and proteins;[54-57] prion inactivation data; the risk of disease transmission with the use of the instrument or device; and a review of other recommendations.[12,16,92,93] Other CJD sterilization recommendations have been based primarily on inactivation studies.[53,77,94]

The 3 parameters integrated into disinfection and sterilization processing for prion-contaminated medical instruments are the patient's risk of having a prion disease, the comparative infectivity of different body tissues, and the intended use of the medical device.[16,92,93] High-risk patients include those with known prion disease; patients with rapidly progressive dementia consistent with possible prion disease; patients with a familial history of CJD, Gerstmann-Straüssler-Scheinker syndrome, or fatal familial insomnia syndrome; patients with a a known mutation in the PrP gene, which is involved in familial TSEs; patients with a history of dura mater transplantation; patients with electroencephalography findings or laboratory evidence suggestive of a TSE (eg, markers of neuronal injury such as 14–3-3 protein); and patients with a known history of cadaver-derived pituitary hormone injection. Tissues at high risk of carrying prions include those of the brain, spinal cord, pituitary gland, and posterior eye (including the retina or optic nerve). All other tissues are considered to have low or no risk (Table 1). Critical devices are any that enter sterile tissue or the vascular system (eg, surgical instruments). Semicritical devices are those that con-

tact nonintact skin or mucous membranes (eg, gastrointestinal endoscopes). The practices recommended by the Association of peri-Operative Registered Nurses and the Association for the Advancement of Medical Instrumentation for reprocessing surgical instruments exposed to CJD are consistent with the following recommendations.[16,95,96]

Recommendations for disinfection and sterilization of prion-contaminated medical devices are as follows. Instruments should be kept wet (eg, immersed in water or a prionicidal detergent) or damp after use and until they are decontaminated, and they should be decontaminated (eg, in an automated washer-disinfector) as soon as possible after use. Dried films of tissue are more resistant to prion inactivation by means of steam sterilization than are tissues that are kept moist. This may be related to the rapid heating that occurs in the film of dried material compared with the bulk of the sample, and to the rapid fixation or dehydration of the prion protein in the dried film.[31] It seems that prions in the dried portions of brain macerates are less efficiently inactivated than prions in undisturbed tissue. In addition, certain disinfectants (eg, glutaraldehyde, formaldehyde, or ethanol) can fix or dehydrate the protein and make it more difficult to inacti vate.[51,69,97,98] A procedure using formalin together with formic acid has been proposed for the preparation of tissue samples obtained from patients with CJD.[99]

The high resistance of prions to standard sterilization methods warrants special procedures in the reprocessing of surgical instruments. Special prion reprocessing is necessary when reprocessing critical or semicritical medical devices that have had contact with high-risk tissues from high-risk patients. After the device is clean, it should be sterilized by either autoclaving (ie, steam sterilization) or using a combination of sodium hydroxide and autoclaving,[12] using 1 of the 4 options below:

Option 1. Autoclave at 134°C for 18 minutes in a prevacuum sterilizer.

Option 2. Autoclave at 132°C for 1 hour in a gravity displacement sterilizer.

Option 3. Immerse in 1 N NaOH (1 N NaOH is a solution of 40 g NaOH in 1 L water) for 1 hour; remove and rinse in water, then transfer to an open pan and autoclave (121°C gravity displacement sterilizer or 134°C porous or prevacuum sterilizer) for 1 hour.

Option 4. Immerse in 1 N NaOH for 1 hour and heat in a gravity displacement sterilizer at 121°C for 30 minutes, then clean and subject to routine sterilization.

Some data suggest that the temperature should not exceed 134°C, since under certain conditions the effectiveness of autoclaving actually declines as the temperature is increased (eg, to 136°C or 138°C),[52] but other data do not demonstrate reduced effectiveness with increasing temperature (eg, 138°C).[69] While 6 options were included in the World Health Organization conference of 1999, in the current recommendations we have included only those options for which scientific studies have best demonstrated both safety (for equipment and operator) and efficacy. It is unclear from the published literature which of these options is the best for complete inactivation of prions, because some studies have revealed excellent but not complete inactivation of the test prions with autoclaving only (options 1 and 2) and the same result for use of NaOH and autoclaving (options 3 and 4). This is likely explained by methodological differences between the studies, but the studies that used the same method for evaluating both autoclaving (option 1) and use of NaOH plus autoclaving (option 3) revealed similar results.[29,30,32,33,89]

It is essential with any sterilization process, and especially when prion-contaminated devices are involved, that the instrument be fully accessible to the sterilant (eg, steam).[30] Prion-contaminated medical devices that are impossible to clean or fully expose to steam and other sterilants should be discarded. Flash sterilization should not be used for reprocessing. Always discard single-use devices. To minimize environmental contamination, noncritical environmental surfaces should be covered with plastic-backed paper, and if the paper has been contaminated with high-risk tissues, it should be properly discarded (eg, as nonregulated medical waste). There are no antimicrobial products registered by the Environmental Protection Agency (EPA) specifically for inactivation of prions on environmental surfaces, and there are no sterilization processes cleared by the Food and Drug Administration for sterilization of reusable surgical instruments. However, the EPA has issued quarantine exemptions to several states that permit the temporary use of a phenolic (containing 6.4% ortho-benzyl-para-chlorophenol, 3.0% para-tertiary-amylphenol, 0.5% ortho-phenyl phenol, 4.9% hexylene glycol, 12.6% glycolic acid, and 8% isopropanol)[81] for inactivation of prions on hard, nonporous surfaces in laboratories that handle contaminated or potentially contaminated animal tissues and wastes. If no EPA-registered or exempted products are available, then noncritical environmental surfaces (eg, laboratory surfaces) contaminated with high-risk tissues (eg, brain tissue) should be cleaned and then spot decontaminated with a 1 : 5 to 1 : 10 dilution of hypochlorite solutions, ideally for a contact time of at least 15 minutes.[42-44,79,83,84,100]

No recommendation can be made regarding the use of special prion reprocessing for reprocessing critical or semicritical devices contaminated with low-risk tissues from high-risk patients. Although low-risk tissue has been found to transmit CJD at a low frequency (Table 1), this has been demonstrated only when low-risk tissue is inoculated into the brain of a susceptible animal. In humans, medical instruments contaminated with low-risk tissue would be unlikely to transmit infection after standard cleaning and sterilization, since the instruments would not be used in the central nervous system. Environmental surfaces contaminated with low-risk tissues from high-risk patients require only standard disinfection.[16,92,93] Since noncritical surfaces are not involved in disease transmission, the normal exposure time ($\geqslant$1 minute) is recommended.[101]

To minimize the possibility of using neurosurgical instruments that potentially were contaminated during procedures performed on patients in whom CJD was later diagnosed, healthcare facilities should consider using the sterilization guidelines outlined below for neurosurgical instruments used during brain biopsy performed on patients in whom a specific lesion (eg, a suspected tumor or abscess) has not been demonstrated (eg, by magnetic resonance imaging or computed tomography scans). Alternatively, disposable neurosurgical instruments should be used for such patients,[16] or the instruments could be quarantined until the pathologic findings of the brain biopsy are reviewed and the diagnosis of CJD is excluded. If disposable instruments are used, they should be of the same quality as reusable devices. Some countries (eg, France and Switzerland) have implemented enhanced sterilization rules to prevent the transmission of CJD by means of surgical instruments, requiring steam sterilization at 134°C for 18 minutes for all surgical instruments. Other countries (eg, United Kingdom) discard all surgical instruments used on high-risk tissues from patients known to have CJD.[64]

When a neuropathologic diagnosis of unsuspected CJD is made on the basis of a brain biopsy or at the time of autopsy, instruments used on high-risk tissues of the patient should be recalled and reprocessed using special prion reprocessing methods. To enhance the ability to recall such instruments, ideally institutions should have a tracking system in place that permits recall of critical or semicritical devices used on high-risk tissue and high-risk patients. This tracking system should permit identification of the patient on which the devices were used, the date they were used, the procedure performed, and the surgeon's name.[96] The decision whether to notify patients on whom such instruments were used should be based on an analysis of the risk of CJD transmission.[102-104]

Most of the data that form the basis of these recommendations have been generated from studies of the prions responsible for sporadic CJD, vCJD, or animal TSE diseases (eg, scrapie and bovine spongiform encephalopathy). To date, there have been no reports of human-to-human transmission of vCJD by tissue, but 4 possible cases of vCJD transmitted by blood transfusion have been reported.[105-108] Unlike sporadic CJD, patients with vCJD have infectivity detectable in lymphoid tissue, such as the appendix, spleen, tonsils, thymus, and lymph nodes. Furthermore, vCJD infectivity may be detectable before the onset of clinical illness. Prion contamination of medical instruments has raised concern about the possible human-to-human transmission of vCJD by medical instruments contaminated with such tissues. On the basis of these concerns, the use of prion disinfection and sterilization guidelines (or use of single-use instruments) has been proposed in the United Kingdom for instruments used in dental procedures,[40,109] eye procedures,[110] or tonsillar surgery[111] on patients at high risk of having sporadic CJD or vCJD. Following complications (death in 1 patient and increased bleeding [1% with reusable instruments vs 12% for disposable instruments]) associated with the use of single-use instruments in tonsillar surgery,[112] it is now advised in the United Kingdom that, given the balance of risk, surgeons can return to using reusable surgical equipment. If epidemiologic and infectivity data show that these tissues represent a transmission risk, then CJD sterilization precautions (or use of disposable equipment) could be extended to equipment used for these procedures.[113]

STANDARD PRECAUTIONS TO PREVENT TRANSMISSION FROM PRION-CONTAMINATED INSTRUMENTS

During the past 10 years, many researchers have searched for a method that inactivates prions on medical instruments yet can be applied to all instrument reprocessing so that special prion reprocessing would not be necessary.[17,64] Some products (eg, alkaline detergents) have been independently certified by the European Community Notified Body, which means that the product has a "CE" marking but the manufacturer is relied on to assess the scientific qualities of the product.[40] Thus, the use of these products remains at the discretion of users, and the users should use detergents that have been shown to reduce infectivity.[17,27-,32,60-64] However, it seems that a number of alkaline and enzymatic detergents have proved to be as effective in eliminating prion infectivity as is 1 N NaOH, the method recommended by the World Health Organization.[48] The practical application of an alkaline detergent in a washer-disinfector followed by steam sterilization has been investigated and shown to eliminate prions from steel surfaces.[64] Ideally, this research will continue and will demonstrate the suitability of integrating new alkaline or enzymatic detergents into the current mechanical washers (eg, washer-disinfectors) in central processing departments, so that the inactivation provided by the detergent (ie, a 5–6 $\log_{10}$ reduction in infectivity) added to the reduction offered by the sterilization process (eg, steam sterilization, 5–6 $\log_{10}$ reduction) would eliminate the risks of transmitting infection by way of prion-contaminated medical or surgical instruments. When this goal is achieved, the need for special prion reprocessing will be eliminated. Until that time, this guideline should be updated periodically so that new methods of removing or inactivating prions from medical devices and new disinfection and sterilization practices can be included.

GENERAL INFECTION PREVENTION PRECAUTIONS

Standard precautions should be used for all patients with known or suspected CJD. Additional precautions (eg, contact precautions) are unnecessary. Gloves should be worn for handling of blood and body fluids. Masks, gowns, and protective eyewear should be worn if mucous membrane or skin exposure to blood or other material that is potentially infectious is anticipated. Laundry should be managed as required by the Occupational Safety and Health Administration (OSHA)

TABLE 4. Categorization of Recommendations

Category	Definition
Category IA	Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.
Category IB	Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies, and a strong theoretical rationale.
Category II	Suggested for implementation and supported by suggestive clinical or epidemiologic studies or by a theoretical rationale.
No recommendation	Unresolved issue. Practices for which insufficient evidence or no consensus exists regarding efficacy.

rule on bloodborne pathogens.[114] No additional precautions are required. No special precautions are required for the handling of food utensils. Patients with known or suspected prion disease should not serve as donors for organs, tissues, blood components, or sources of tissue (eg, dura mater and hormones).

The use of standard precautions in central processing departments, in clinical laboratories, or during the processing of pathologic materials (including during autopsy) should preclude any possibility of CJD transmission to healthcare personnel. Thus, there is no need to decontaminate or discard instruments (eg, a washer-disinfector or a cerebrospinal fluid analyzer) whose internal components may have been contaminated with prions. However, external surfaces that are contaminated with high-risk tissue should be decontaminated as described.

No special precautions are required for the disposal of body fluids. Such fluids may be disposed of by means of a sanitary sewer. Disposable sheets used to cover work surfaces may be disposed of as nonregulated medical waste. Regulated medical waste (eg, bulk blood, pathologic waste, or sharp devices) should be managed according to state regulations. When a patient dies, ensure that the morgue and funeral home are notified that the patient had CJD. No excess precautions need to be taken with regard to burial (eg, no special cemetery is required).

There is no evidence of occupational transmission of CJD to a healthcare worker. Although cases of CJD have been reported in healthcare workers, the incidence does not exceed what would be expected from chance alone.[115] In the context of occupational exposure, the highest potential risk results from exposure to high-infectivity tissue through needlestick injuries with inoculation. Percutaneous exposure to the cerebrospinal fluid or brain tissue of an infected person can be followed by washing with detergent and copious water (avoid scrubbing), rinsing, and drying, although scientifically unproven to reduce risk. For maximum safety, consider briefly rinsing the wound with 0.5% sodium hypochlorite (or another chemical with prionicidal activity) and then rinsing with water. Mucous membrane exposure to infectious tissues or fluids should be managed by irrigating the mucous membrane thoroughly with saline for several minutes.

RECOMMENDATIONS FOR PROCESSING CJD-CONTAMINATED PATIENT-CARE EQUIPMENT AND ENVIRONMENTAL SURFACES

This section does not apply to vCJD.

We have used the system for categorizing the strength of recommendations that is currently used by the Centers for Disease Control and Prevention for Healthcare Infection Control Practices Advisory Committee recommendations (see Table 4).

A. Do not allow instruments to become dry after use. Dried films of tissue are more resistant to prion inactivation by steam sterilization than are tissues that have been kept moist. Keep instruments moist (either wet by immersion in water or a detergent with prionicidal activity or, if not possible, by use of a wet cloth draped over the instruments or use of a transport gel or foam) after use and during storage or transport prior to decontamination in central processing departments. Instruments should be decontaminated as soon as possible after use. Decontaminate instruments in a mechanical washer (eg, washer-disinfector) with a detergent (preferably a detergent that has been shown to have prionicidal activity), and after decontamination, sterilize by one of the methods shown to be effective and recommended below.[17,27-,55-57,59-64,101] (Category IA.)

B. Use the following recommended procedures (see recommendations 1–10 below) to reprocess critical or semicritical items that have been contaminated with high-risk tissues (defined as brain [including dura mater], spinal cord, posterior eye, and pituitary tissue) from high-risk patients (eg, those with known or suspected CJD).[11-16,18,19,24,27,29,30,32,33,37,40,42,44,45,47,48,53,60,64,69,77,78,81,83,84,89,90,92-96,100(Appendix D),116] (Category IB.)

1. Clean devices (eg, surgical instruments) that have been constructed so that cleaning procedures result in effective tissue removal and then sterilize these devices by one of the following methods (listed in order of effectiveness as supported by the scientific literature). (Category 1B.)

Option 1. Autoclave at 134°C for ⩾18 minutes in a prevacuum sterilizer.[27-30,32,33,37,44,45,51,52]

Option 2. Autoclave at 132°C for 1 hour in a gravity displacement sterilizer.[43,47,83,89,98]

Option 3. Immerse in 1 N NaOH for 1 hour; remove and rinse in water, then transfer to an open pan and autoclave (121°C in a gravity displacement sterilizer or 134°C in a porous or prevacuum sterilizer) for 1 hour.[29,32,33,41,47,89]

Option 4. Immerse instruments in 1 N NaOH for 1 hour and heat in a gravity displacement sterilizer at 121°C for 30 minutes (to minimize autoclave and operator exposure to gaseous NaOH when immersing instruments and autoclaving in NaOH, the use of containers with a rim and lid designed for condensation to collect and drip back into the pan is recommended); then rinse and subject to routine sterilization.[90]

2. Discard devices that are impossible to clean.[16,57] (Category II.)

3. Do not use flash sterilization for reprocessing instruments.[16,101] (Category IB.)

4. Discard items that permit only low-temperature sterilization (eg, sterilization with ethylene oxide).[84] (Category IB.)

5. No recommendation can be made regarding the use of low-temperature technologies that have shown prionicidal activity, such as a specific type of hydrogen peroxide gas plasma and vaporized hydrogen peroxide, as the data are limited and require corroboration.[27,32,36] (No recommendation: unresolved issue.)

6. Recall contaminated items (eg, medical devices used for brain biopsy before diagnosis) that have not been processed according to these recommendations and appropriately reprocess them.[16,101] (Category II.)

7. To minimize patient exposure to neurosurgical instruments later determined to have been used on a patient with CJD, use the sterilization guidelines above for neurosurgical instruments used on patients undergoing brain biopsy when a specific lesion (eg, a suspected tumor or abscess) has not been demonstrated (by computed tomography or magnetic resonance imaging). Alternatively, use disposable neurosurgical instruments on such patients.[16] (Category IB.)

8. Clean noncritical environmental surfaces contaminated with high-risk tissues (eg, a laboratory surface in contact with brain tissue of a CJD-infected person) with a detergent and then spot decontaminate these surfaces with a 1 : 5 to 1 : 10 dilution of sodium hypochlorite (ie, bleach; a 1 : 5 dilution of 5.25%–6.15% sodium hypochlorite provides 10,500–12,300 ppm chlorine), ideally for a contact time of at least 15 minutes. To minimize environmental contamination, use disposable plastic-backed cover sheets on work surfaces.[42-44,78,79,83,84,100] (Category IB.)

9. Clean and then disinfect noncritical equipment that has been contaminated with high-risk tissue using a 1 : 5 to 1 : 10 dilution of sodium hypochlorite or 1 N NaOH, depending on material compatibility. Ensure that all contaminated surfaces are exposed to the disinfectant.[42-44,79,83,84,100] (Category IB.)

10. If the operating surgeon believes that the patient is at risk for a TSE such as CJD, he or she should communicate that information to the operating room charge nurse, the anesthesiology staff, the neuropathology or clinical pathology laboratory staff, the risk manager, and the infection preventionist. Train clinicians and reprocessing technicians on how to properly tag the equipment and train them in the special prion reprocessing protocols. Because standard decontamination of tissue samples (eg, with formalin) or specimens may not inactivate CJD, all tissue samples should be handled with the use of standard precautions (ie, gloves). Tag equipment that requires special prion reprocessing after use. The tissue samples and specimens should be labeled as a "biohazard" and as "suspected CJD" before being sent to the laboratory.[16] (Category IB.)

C. No recommendation can be made regarding the use of the procedures listed in recommendation B1–B10 for reprocessing of critical or semicritical medical devices that have been contaminated with low-risk tissues (defined as cerebrospinal fluid, kidney, liver, spleen, lung, placenta, olfactory epithelium, and lymph nodes) from high-risk patients. (No recommendation: unresolved issue.)

D. Use only standard disinfection to process environmental surfaces contaminated with low-risk tissues. (Use disinfectants recommended by OSHA for disinfecting blood-contaminated surfaces.)[53,101,114] (Category IB.)

E. Use the following recommended procedures to reprocess critical or semicritical medical devices that have been contaminated with no-risk tissue (defined as peripheral nerve, intestine, bone marrow, blood, leukocytes, serum, thyroid gland, adrenal gland, heart, skeletal muscle, adipose tissue, gingiva, prostate, testis, tears, saliva, sputum, urine, feces, semen, vaginal secretions, milk, sweat) from high-risk patients.[12,15,16,18,20,53,101,114] (Category IB.)

1. Clean and either disinfect or sterilize these devices using conventional protocols of heat or chemical sterilization or high-level disinfection. (Category IB.)

2. Use standard cleaning and high-level disinfection protocols for reprocessing endoscopes (except neurosurgical endoscopes with central nervous system contact), because these devices can become contaminated only with no-risk materials. (Category IB.)

3. Use standard disinfection to process noncritical equipment and noncritical environmental surfaces that have been contaminated with no-risk tissues or fluids

(use disinfectants recommended by OSHA for decontaminating blood-contaminated surfaces [eg, 1 : 10 to 1 : 100 dilution of 5.25%–6.15% sodium hypochlorite]). (Category IB.)

F. A quality control program should be established and maintained that enhances healthcare worker performance (orientation, continuing education, and documented competency) and monitors disinfection and sterilization efficacy (eg, sterilizer maintenance and repair history; sterilization process monitoring by means of physical, chemical, and biological monitors; and disinfectant concentration).[96,101,117] (Category IB.)

Address reprint requests to William A. Rutala, PhD, MPH, Division of Infectious Diseases, University of North Carolina School of Medicine, Chapel Hill, NC 27599-7030 (brutala@unch.unc.edu).

REFERENCES

1. Centers for Disease Control and Prevention (CDC). Surveillance for Creutzfeldt-Jakob disease—United States. *MMWR Morb Mortal Wkly Rep* 1996;45:665–668.
2. Johnson RT, Gibbs CJ Jr. Creutzfeldt-Jakob disease and related transmissible spongiform encephalopathies. *N Engl J Med* 1998;339:1994–2004.
3. Collins SJ, Lawson VA, Masters CL. Transmissible spongiform encephalopathies. *Lancet* 2004;363:51–61.
4. Belay ED, Sejvar JJ, Shieh W-J, et al. Variant Creutzfeldt-Jakob disease death, United States. *Emerg Infect Dis* 2005;11:1351–1354.
5. Centers for Disease Control and Prevention (CDC). Probable variant Creutzfeldt-Jakob disease in a U.S. resident—Florida, 2002. *MMWR Morb Mortal Wkly Rep* 2002;51:927–929.
6. National Creutzfeldt-Jakob Disease Surveillance Unit. Variant Creutzfeldt-Jakob Diseases Current Data, July 2009. Edinburgh, Scotland: University of Edinburgh; 2009.
7. Belay ED, Maddox RA, Williams ES, Miller MW, Gambetti P, Schonberger LB. Chronic wasting disease and potential transmission to humans. *Emerg Infect Dis* 2004;10:977–984.
8. Kong Q, Huang S, Zou W, et al. Chronic wasting disease of elk: transmissibility to humans examined by transgenic mouse models. *J Neurosci* 2005;25:7944–7949.
9. Centers for Disease Control and Prevention (CDC). Fatal degenerative neurologic illnesses in men who participated in wild game feasts—Wisconsin, 2002. *MMWR Morb Mortal Wkly Rep* 2003;52:125–127.
10. Mawhinney S, Pape WJ, Forster JE, Anderson CA, Bosque P, Miller MW. Human prion disease and relative risk associated with chronic wasting disease. *Emerg Infect Dis* 2006;12:1527–1535.
11. Brown P, Brandel J-P, Preese M, Sato T. Iatrogenic Creutzfeldt-Jakob disease: the waning of an era. *Neurology* 2006;67:389–393.
12. World Health Organization (WHO). WHO infection control guidelines for transmissible spongiform encephalopathies. Geneva, Switzerland: WHO; 2000. Available at: http://www.who.int/csr/resources/publications/bse/whocdscsraph2003.pdf. Accessed January 3, 2010.
13. Brown P, Preece M, Brandel JP, et al. Iatrogenic Creutzfeldt-Jakob disease at the millennium. *Neurology* 2000;55:1075–1081.
14. Brown P. Environmental causes of human spongiform encephalopathy. In: Baker H, Ridley RM, eds. *Methods in Molecular Medicine: Prion Diseases.* Totowa, NJ: Humana Press; 1996:139–154.
15. Brown P, Gibbs CJ, Rodgers-Johnson P, et al. Human spongiform encephalopathy: the National Institutes of Health series of 300 cases of experimentally transmitted disease. *Ann Neurol* 1994;35:513–529.
16. Rutala WA, Weber DJ. Creutzfeldt-Jakob disease: recommendations for disinfection and sterilization. *Clin Infect Dis* 2001;32:1348–1356.
17. McDonnell G. Prion disease transmission: Can we apply standard precautions to prevent or reduce risks? *J Perioper Pract* 2008;18:298–304.
18. Tamai Y, Kojima H, Kitajima R, et al. Demonstration of the transmissible agent in tissue from a pregnant woman with Creutzfeldt-Jakob disease. *N Engl J Med* 1992;327:649.
19. Zanusso G, Ferrari S, Cardone F, et al. Detection of pathologic prion protein in the olfactory epithelium in sporadic Creutzfeldt-Jakob disease. *N Engl J Med* 2003;348:711–719.
20. Geertsma RE, van Asten JAAM. Sterilization of prions: requirements, complications, implications. *Zentralbl Steril* 1995;3:385–394.
21. Bernoulli C, Siegfried J, Baumgartner G, et al. Danger of accidental person-to-person transmission of Creutzfeldt-Jakob disease by surgery. *Lancet* 1977;1(8009):478–479.
22. Nevin S, McMenemey WH, Behrman S, Jones DP. Subacute spongiform encephalopathy—a subacute form of encephalopathy attributable to vascular dysfunction (spongiform cerebral atrophy). *Brain* 1960;83:519–569.
23. Foncin J-F, Gaches J, Cathala F, Sherif E, LeBeau J. Transmission iatrogène interhumaine possible de maladie de Creutzfeldt-Jakob avec atteinte des grains du cervelet. *Rev Neurol (Paris)* 1980;136:280.
24. Barash JA, Johnson BT, Gregorio DI. Is surgery a risk factor for Creutzfeldt-Jakob disease? Outcome variations by control choice and exposure assessments. *Infect Control Hosp Epidemiol* 2008;29:212–218.
25. Hamaguchi T, Noguchi-Shinohara M, Nakamura Y, et al. Ophthalmic surgery in prion diseases. *Emerg Infect Dis* 2007;13:162–164.
26. Chamberland ME. Emerging infectious agents: do they pose a risk to the safety of transfused blood and blood products? *Clin Infect Dis* 2002; 34:797–805.
27. Fichet G, Comoy C, Duval C, et al. Novel methods for disinfection of prion-contaminated medical devices. *Lancet* 2004;364:521–526.
28. Fichet G, Comoy E, Dehen C, et al. Investigations of a prion infectivity assay to evaluate methods of decontamination. *J Microbiol Methods* 2007;70:511–518.
29. Yan ZX, Stitz L, Heeg P, Roth K, Mauz P-S. Low-temperature inactivation of prion-protein on surgical steel surfaces with hydrogen peroxide gas plasma sterilization. *Zentralbl Steril* 2008;16:26–34.
30. Jackson GS, McKintosh E, Flechsig E, et al. An enzyme-detergent method for effective prion decontamination of surgical steel. *J Gen Virol* 2005;86:869–878.
31. Taylor DM. Inactivation of transmissible degenerative encephalopathy agents: a review. *Vet J* 2000;159:10–17.
32. Rogez-Kreuz C, Yousfi R, Soufflet C, et al. Inactivation of animal and human prions by hydrogen peroxide gas plasma sterilization. *Infect Control Hosp Epidemiol* 2009;30:769–777.
33. Yan Z, Stitz L, Heeg P, Pfaff E, Roth K. Infectivity of prion protein bound to stainless steel wires: a model for testing decontamination procedures for transmissible spongiform encephalopathies. *Infect Control Hosp Epidemiol* 2004;25:280–283.
34. Solassol J, Arlotto M, Lehmann S. Detection of prion after decontamination procedures: comparative study of standard Western blot, filter retention, and scrapie-cell assay. *J Hosp Infect* 2004;57:156–161.
35. Rutala WA, Weber DJ. Management of equipment contaminated with Creutzfeldt-Jakob disease. In: Rutala WA, ed. *Disinfection, Sterilization and Antisepsis: Principles and Practices in Healthcare Facilities.* Washington, DC: Association for Professionals in Infection Control and Epidemiology; 2001:167–172.
36. Fichet G, Antloga K, Comoy E, Deslys JP, McDonnell G. Prion inactivation using a new gaseous hydrogen peroxide sterilization process. *J Hosp Infect* 2007;67:278–286.
37. Peretz D, Supattapone S, Giles K, et al. Inactivation of prions by acidic sodium dodecyl sulfate. *J Virol* 2006;80:322–331.
38. Dickinson AG, Taylor DM. Resistance of scrapie agent to decontamination. *N Engl J Med* 1978;299:1413–1414.

39. Hartley EG. Action of disinfectants on experimental mouse scrapie. *Nature* 1967;213:1135.
40. Walker JT, Dickinson J, Sutton JM, Marsh PD, Raven NDH. Implications for Creutzfeldt-Jakob disease (CJD) in dentistry: a review of current knowledge. *J Dent Res* 2008;87:511–519.
41. Taylor DM, Fernie K, McConnell I. Inactivation of the 22A strain of scrapie agent by autoclaving in sodium hydroxide. *Vet Microbiol* 1997; 58:87–91.
42. Brown P, Rohwer RG, Green EM, Gajdusek DC. Effect of chemicals, heat, and histopathologic processing on high-infectivity hamster-adapted scrapie virus. *J Infect Dis* 1982;145:683–687.
43. Kimberlin RH, Walker CA, Millson GC, et al. Disinfection studies with two strains of mouse-passaged scrapie agent: guidelines for Creutzfeldt-Jakob and related agents. *J Neurol Sci* 1983;59:355–369.
44. Taylor DM, Fraser H, McConnell I, et al. Decontamination studies with the agents of bovine spongiform encephalopathy and scrapie. *Arch Virol* 1994;139:313–326.
45. Vadrot C, Darbord J-C. Quantitative evaluation of prion inactivation comparing steam sterilization and chemical sterilants: proposed method for test standardization. *J Hosp Infect* 2006;64:143–148.
46. Baxter HC, Campbell GA, Whittaker AG, et al. Elimination of transmissible spongiform encephalopathy infectivity and decontamination of surgical instruments by using radio-frequency gas-plasma treatment. *J Gen Virol* 2005;86:2393–2399.
47. Ernst DR, Race RE. Comparative analysis of scrapie agent inactivation methods. *J Virol Methods* 1993;41:193–201.
48. Sutton JM, Dickinson J, Walker JT, Raven NDH. Methods to minimize the risks of Creutzfeldt-Jakob disease transmission by surgical procedures: where to set the standard? *Clin Infect Dis* 2006;43:757–764.
49. Zobeley E, Flechsig E, Cozzio A, Enari M, Weissmann C. Infectivity of scrapie prions bound to a stainless steel surface. *Mol Med* 1999;5:240–243.
50. Taylor DM, Diprose MF. The response of the 22A strain of scrapie agent to microwave irradiation compared to boiling. *Neuropathol Appl Neurobiol* 1996;22:256–258.
51. Taylor DM, McConnell I. Autoclaving does not decontaminate formol-fixed scrapie tissues. *Lancet* 1988;1(8600):1463–1464.
52. Taylor DM. Inactivation of prions by physical and chemical means. *J Hosp Infect* 1999;43 (Suppl):S69-S76.
53. Rutala WA; 1994, 1995, and 1996 APIC Guidelines Committee. APIC guideline for selection and use of disinfectants. Association for Professionals in Infection Control and Epidemiology. *Am J Infect Control* 1996; 24:313–342.
54. Rutala WA, Weber DJ. FDA labeling requirements for disinfection of endoscopes: a counterpoint. *Infect Control Hosp Epidemiol* 1995;16:231–235.
55. Merritt K, Hitchins VM, Brown SA. Safety and cleaning of medical materials and devices. *J Biomed Mater Res* 2000;53:131–136.
56. Alfa MJ, Jackson M. A new hydrogen peroxide-based medical-device detergent with germicidal properties: comparison with enzymatic cleaners. *Am J Infect Control* 2001;29:168–177.
57. Jacobs P. Cleaning: principles, methods and benefits. In: Rutala WA, ed. *Disinfection, Sterilization, and Antisepsis in Healthcare.* Champlain, NY: Polyscience Publications; 1998:165–181.
58. Stephenson J. Halting the spread of human prion disease—exceptional measures for an exceptional problem. *J Hosp Infect* 2007;65:14–18.
59. Lipscomb IP, Pinchin H, Collin R, Kevil CW. Effect of drying time, ambient temperature and pre-soaks on prion-infected tissue contamination levels on surgical stainless steel: concerns over prolonged transportation of instruments from theatre to central sterile service departments. *J Hosp Infect* 2007;65:72–77.
60. Baier M, Schwarz A, Mielke M. Activity of an alkaline 'cleaner' in the inactivation of the scrapie agent. *J Hosp Infect* 2004;57:80–84.
61. Yoshioka M, Murayama Y, Miwa T, et al. Assessment of prion inactivation by combined use of *Bacillus*-derived protease and SDS. *Biosci Biotechnol Biochem* 2007;71:2565–2568.
62. Lawson VA, Stewart JD, Masters CL. Enzymatic detergent treatment protocol that reduces protease-resistant prion load and infectivity from surgical-steel monofilaments contaminated with a human-derived prion strain. *J Gen Virol* 2007;88:2905–2914.
63. United Kingdom Department of Health. New technologies working group report on prion inactivating agents. London, UK: Department of Health; 2008:1–30.
64. Fichet G, Harrison J, McDonnell G. Reduction of risk of prion transmission on surgical devices with effective cleaning processes. *Zentralbl Steril* 2007;15:418–437.
65. McLeod AH, Murdoch H, Dickinson J, et al. Proteolytic inactivation of the bovine spongiform encephalopathy agent. *Biochem Biophys Res Commun* 2004;317:1165–1170.
66. McDonnell G, Fichet G, Kaiser H, et al. Cleaning investigations to reduce the risk of prion contamination on manufacturing surfaces and materials. *Eur J Parenter Pharm Sci* 2005;10:67–72.
67. Dickinson J, Murdoch H, Dennis MJ, et al. Decontamination of prion protein (BSE301V) using a genetically engineered protease. *J Hosp Infect* 2009;72:65–70.
68. Rohwer RG. Virus like sensitivity of the scrapie agent to heat inactivation. *Science* 1984;223:600–602.
69. Fernie K, Steele PJ, Taylor DM, Somerville RA. Comparative studies on the thermostability of five strains of transmissible-spongiform-encephalopathy agent. *Biotechnol Appl Biochem* 2007;47:175–183.
70. Murdoch H, Taylor D, Dickinson J, et al. Surface decontamination of surgical instruments: an ongoing dilemma. *J Hosp Infect* 2006;63:432–438.
71. Sattar SA, Springthorpe VS. New methods for efficacy testing of disinfectants and antiseptics. In: Rutala WA, ed. *Disinfection, Sterilization and Antisepsis: Principles and Practices in Healthcare Facilities.* Washington, DC: Association for Professionals in Infection Control and Epidemiology; 2001:174–186.
72. McDonnell G, Amato R, Malchesky PS, Muzic DS, Marchant RE. Use of Dacron as an alternative for evaluating oxidizing sterilants in the AOAC sporicidal tests. *J AOAC Int* 2000;83:269–275.
73. Ascenzi JM, Ezzell RJ, Wendt TM. A more accurate method for measurement of tuberculocidal activity of disinfectants. *Appl Environ Microbiol* 1987;53:2189–2192.
74. Rutala WA, Cole EC. Ineffectiveness of hospital disinfectants against bacteria: a collaborative study. *Infect Control* 1987;8:501–506.
75. Cole EC, Rutala WA, Alfano EM. Comparison of stainless steel penicylinders used in disinfectant testing. *J Assoc Off Anal Chem* 1988;71: 288–289.
76. Cole EC, Rutala WA, Nessen L, Wannamaker NS, Weber DJ. Effect of methodology, dilution, and exposure time on the tuberculocidal activity of glutaraldehyde-based disinfectants. *Appl Environ Microbiol* 1990;56: 1813–1817.
77. Steelman VM. Activity of sterilization processes and disinfectants against prions (Creutzfeldt-Jakob disease agent). In: Rutala WA, ed. *Disinfection, Sterilization, and Antisepsis in Healthcare.* Champlain, NY: Polyscience Publications; 1998:255–271.
78. Flechsig E, Hegyi I, Enari M, Schwarz P, Collinge J, Weissmann C. Transmission of scrapie by steel-surface-bound prions. *Mol Med* 2001;7: 679–684.
79. Lemmer K, Mielke M, Pauli G, Beekes M. Decontamination of surgical instruments from prion proteins: *in vitro* studies on the detachment, destabilization and degradation of PrP^{sc} bound to steel surfaces. *J Gen Virol* 2004;85:3805–3816.
80. Langeveld JPM, Wang JJ, Van de Wiel DFM, Shih GC, et al. Enzymatic degradation of prion protein in brain stem from infected cattle and sheep. *J Infect Dis* 2003;188:1782–1789.
81. Race RE, Raymond GJ. Inactivation of transmissible spongiform encephalopathy (prion) agents by Environ LpH. *J Virol* 2004;78:2164–2165.
82. Riemer C, Bamme T, Mok SWF, Baier M. 3-methyl-4-chlorophenol for

prion decontamination of medical devices. *Infect Control Hosp Epidemiol* 2006;27:778–780.
83. Brown P, Rohwer RG, Gajdusek DC. Newer data on the inactivation of scrapie virus or Creutzfeldt-Jakob disease virus in brain tissue. *J Infect Dis* 1986;153:1145–1148.
84. Brown P, Gibbs CJ Jr, Amyx HL, et al. Chemical disinfection of Creutzfeldt-Jakob disease virus. *N Engl J Med* 1982;306:1279–1282.
85. Solassol J, Pastore M, Crozet C, Perrier V, Lehmann S. A novel copper-hydrogen peroxide formulation for prion decontamination. *J Infect Dis* 2006;194:865–869.
86. Manuelidis L. Decontamination of Creutzfeldt-Jakob disease and other transmissible agents. *J Neurovirol* 1997;3:62–65.
87. Tateishi J, Tashima T, Kitamoto T. Practical methods for chemical inactivation of Creutzfeldt-Jakob disease pathogen. *Microbiol Immunol* 1991;35:163–166.
88. Taylor DM. Resistance of the ME7 scrapie agent to peracetic acid. *Vet Microbiol* 1991;27:19–24.
89. Taguchi F, Tamai Y, Uchida A, et al. Proposal for a procedure for complete inactivation of the Creutzfeldt-Jakob disease agent. *Arch Virol* 1991;119:297–301.
90. Brown SA, Merritt K. Use of containment pans and lids for autoclaving caustic solutions. *Am J Infect Control* 2003;31:257–260.
91. Rabano A, de Pedro-Cuesta J, Molbak K, et al. Tissue classification for the epidemiological assessment of surgical transmission of sporadic Creutzfeldt-Jakob disease: a proposal on hypothetical risk levels. *BMC Public Health* 2005;5:9.
92. Favero MS. Current issues in hospital hygiene and sterilization technology. *J Infect Control (Asia Pacific Ed.)* 1998;1:8–10.
93. Favero MS, Bond WW. Chemical disinfection of medical and surgical materials. In: Block SS, ed. *Disinfection, Sterilization, and Preservation.* Philadelphia, PA: Lippincott Williams & Wilkins; 2001:881–917.
94. Committee on Health Care Issues, American Neurological Association. Precautions in handling tissues, fluids, and other contaminated materials from patients with documented or suspected Creutzfeldt-Jakob disease. *Ann Neurol* 1986;19:75–77.
95. Association of periOperative Registered Nurses (AORN). Recommended practices for cleaning and caring for surgical instruments and powered equipment. In: AORN, ed. *Standards, Recommended Practices, and Guidelines.* Denver: AORN; 2006:555–563.
96. Association for the Advancement of Medical Instrumentation (AAMI). Comprehensive guide to steam sterilization and sterility assurance in health care facilities. Arlington, VA: AAMI; 2006:ANSI/AAMI ST79.
97. Kampf G, Blob R, Martiny H. Surface fixation of dried blood by glutaraldehyde and peracetic acid. *J Hosp Infect* 2004;57:139–143.
98. Brown P, Liberski PP, Wolff A, et al. Resistance of scrapie infectivity to steam autoclaving after formaldehyde fixation and limited survival after ashing at 360°C: practical and theoretical implications. *J Infect Dis* 1990; 161:467–472.
99. Brown P, Wolff A, Gajdusek DC. A simple and effective method for inactivating virus infectivity in formalin-fixed tissue samples from patients with Creutzfeldt-Jakob disease. *Neurology* 1990;40:887–890.
100. CLSI. Protection of laboratory workers from occupationally acquired infections; approved guideline—third edition. CLSI document. Wayne, PA: CLSI; 2005:M29-A3.
101. Rutala WA, Weber DJ; Healthcare Infection Control Practices Advisory Committee. Guideline for disinfection and sterilization in healthcare facilities, 2008. Atlanta, GA: CDC. Published November 2008. http://cdc.gov/ncidod/dhqp/pdf/guidelines/Disinfection_Nov_2008.pdf. Accessed January 3, 2010.
102. Rutala WA, Weber DJ. How to assess disease transmission when there is a failure to follow recommended disinfection and sterilization principles. *Infect Control Hosp Epidemiol* 2007;28:519–524.
103. Bourvis N, Boelle P-Y, Cesbron J-Y, Valleron A-J. Risk assessment of transmission of sporadic Creutzfeldt-Jakob disease in endodontic practice in absence of adequate prion inactivation. *PLoS One* 2007;2(12):e1330.
104. Stricof RL, Lillquist PP, Thomas N, Belay ED, Schonberger LB, Morse DL. An investigation of potential neurosurgical transmission of Creutzfeldt-Jakob disease: challenges and lessons learned. *Infect Control Hosp Epidemiol* 2006;27:302–304.
105. Peden AH, Head MW, Ritchie DL, Bell JE, Ironside JW. Preclinical vCJD after blood transfusion in a PRNP codon 129 heterozygous patient. *Lancet* 2004;364:527–529.
106. Llewelyn CA, Hewitt PE, Knight RSG, et al. Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion. *Lancet* 2004;363: 417–421.
107. Wroe SJ, Pal S, Siddique D, et al. Clinical presentation and pre-mortem diagnosis of variant Creutzfeldt-Jakob disease associated with blood transfusion: a case report. *Lancet* 2006;368:2061–2067.
108. Fourth case of transfusion-associated vCJD infection in the United Kingdom. *Euro Surveill* 2007;12(1):E070118.4.
109. Azarpazhooh A, Fillery ED. Prion disease: the implications for dentistry. *J Endod* 2008;34:1158–1166.
110. Tullo A, Buckley R, Painter M. CJD and the eye. *Eye (Lond)* 2000;14: 259–260.
111. Kirkpatrick WNA, Waterhouse N. Pharyngoplasty and the risk of variant CJD transmission. *Br J Plast Surg* 2001;54:552–561.
112. Maheshwar A, De M, Browning ST. Reusable versus disposable instruments in tonsillectomy: a comparative study of outcomes. *Int J Clin Pract* 2003;57:579–583.
113. Weber DJ, Rutala WA. Managing the risk of nosocomial transmission of prion diseases. *Curr Opin Infect Dis* 2002;15:421–425.
114. Occupational Safety and Health Administration. Occupational exposure to bloodborne pathogens; final rule. *Fed Regist* 1991;56:64003–64182.
115. Tyler KL. Prions and prion diseases of the central nervous system (transmissible neurodegenerative diseases). In: Mandell GL, Bennett JE, Dolin R, eds. *Principles and Practices of Infectious Diseases.* Philadelphia: Churchill Livingstone; 2000:1971–1985.
116. Brown P, Will RG, Bradley R, Asher DM, Detwiler L. Bovine spongiform encephalopathy and variant Creutzfeldt-Jakob disease: background, evolution, and current concerns. *Emerg Infect Dis* 2001;7:6–16.
117. Association for peri-Operative Registered Nurses (AORN). Recommended practices for sterilization in the perioperative practice setting. In: AORN, ed. *Standards, Recommended Practices, and Guidelines.* Denver: AORN; 2006:629–643.