Trends in Processing Prion-Contaminated Surgical Instruments

Camila Q.M. Bruna, Rafael Queiroz de Souza, and Kazuko U. Graziano

***Camila Q.M. Bruna**, PhD, RN, is a postdoctoral fellow in the School of Nursing at the University of São Paulo in São Paulo, Brazil. Email: caquartim@yahoo.com.br*
Corresponding author

***Rafael Queiroz de Souza**, PhD, RN, is a professor at Anhanguera University in São Paulo, Brazil. Email: rafaelqsouza@hotmail.com*

***Kazuko U. Graziano**, PhD, RN, is a senior professor in the School of Nursing at the University of São Paulo in São Paulo, Brazil. Email: kugrazia@usp.br*

Abstract

This review sought to provide an overview of proposed methods and protocols for processing surgical instruments contaminated with prions. A search of PubMed was conducted to identify studies published between January 1, 2012, and January 2, 2019, with no language restrictions and using varying combinations of the following terms: prions (Medical Subject Heading [MeSH]) OR decontamination *(MeSH) OR* cleaning *OR* disinfection *OR* sterilization. *Articles were excluded if they did not involve medical device surfaces or describe the processing protocol. At least two reviewers independently selected articles, extracted data, and assessed data. A total of 627 articles published in peer-reviewed journals were identified. Of the 55 articles assessed for full-text eligibility, eight met the inclusion criteria. Only a few studies investigated protocols and methods for processing prion-contaminated medical devices; therefore, determining the best way to sterilize device surfaces and preserve the integrity of surgical instruments remains challenging. Moreover, the perspective of sterile processing department staff continues to be overlooked when designing studies.*

A prion or "proteinaceous infectious particle" is an infectious proteinaceous agent that causes transmissible spongiform encephalopathies (TSEs),[1–3] the most common form of which is sporadic Creutzfeldt-Jakob disease (CJD). CJD has a mortality rate of 1 to 1.5 cases per million each year worldwide.[4] Although rare, the iatrogenic transmission of CJD has been reported previously in relation to the application of prion-contaminated human growth hormone, dura mater grafts, and corneal grafts.

However, few reports show the link between CJD-confirmed cases and prion-contaminated surgical instruments.[4] A 23-year-old female patient and a 17-year-old male patient underwent stereo-electroencephalography using the same electrodes that were used previously for another patient who had a confirmed diagnosis of CJD. Consequently, the two patients died of CJD.[5] The electrodes used for stereo-encephalography were cleaned with benzene and disinfected with 70% ethanol, then stored for two months in a metal box containing 2 g paraformaldehyde. Later, they were applied during a neurological procedure on a chimpanzee that expired after being infected with CJD.[6] A decade later, a 46-year-old male patient died from confirmed CJD following cranial surgery in the same hospital where a female patient had died of confirmed CJD.[7] Another report described cases of mortality following brain surgery, with one death occurring following the removal of two teeth.[8] However, none of these reports could associate the cases of death with the contamination of surgical instruments. Therefore, these reports remain inconclusive.

The high resistance of prions to classic chemical and physical decontamination treatments is well known.[9,10] Inconsistency in eliminating prions from device surfaces, even following the recommended use of extended steam exposure, also has been reported.[11] Instruments that contact high-risk tissue require adequate prion decontamination (using strong alkaline solutions or highly concentrated sodium hypochlorite) to reduce the risk to patients who are subsequently treated with these instruments.[12,13] However, these decontamination protocols can damage device surfaces[14]; therefore, a substantial number of novel disinfectants and processing protocols have been tested and studied to eliminate the risk of CJD transmission via surgical instruments.

Objective

This review sought to provide an overview of methods and protocols for processing surgical instruments contaminated with prions in reports published during a seven-year period.

Methods

This systematic review of the scientific literature was conducted to assess procedures for eliminating prions from the surfaces of surgical instruments. A PubMed search was performed to identify articles published between January 1, 2012, and January 2, 2019, on processing prion-contaminated medical devices. Different combinations of the following terms were used in the literature search: *prions* (Medical Subject Heading [MeSH]) OR *decontamination* (MeSH) OR *cleaning* OR *disinfection* OR *sterilization*. We did not apply language restrictions on the search (Figure 1).

One author (C.Q.M.B.) screened article titles and abstracts and excluded irrelevant search items. Then, the remaining titles with abstracts were screened for eligibility by two authors independently (C.Q.M.B. and R.Q.S.). Next, these two authors independently screened full-text articles and extracted data (e.g., citation, device surface used, type and amount of inoculum, processing methods used, outcome). Disagreements were resolved through consensus-based discussion between the reviewers. Articles were excluded if they did not involve device surfaces or if the processing protocol was not described.

Results

In the initial search, 627 articles published in peer-reviewed journals during 2012–19 were identified (Figure 1). Of the 55 articles assessed for full-text eligibility, eight met the inclusion criteria and 47 were excluded because the study (1) involved biological surfaces, such as cells, rather than device surfaces or (2) did not describe the processing protocol. The results of the identified processing protocols used for decontamination of prion-contaminated device surfaces and their outcomes are described in Table 1.

Discussion

To the authors' knowledge, no previously published review has assessed the processing of prion-contaminated surgical instruments. The results of the current review suggested that because the number of studies on processing methods of prion-contaminated instruments is small, leading practices for completely eliminating prions from surfaces and preserving the integrity of surgical instruments cannot be determined. Studies have focused on using materials other than stainless steel as the outer surface material of surgical instruments. Reports have shown that in the precleaning step, chemicals with known risks to the longevity of surgical instruments were used. These studies were associated with various shortcomings, including being written solely from the laboratory viewpoint and not considering the perspective of sterile processing department (SPD) staff. The lack of a practice-based perspective can lead to limitations in the application of the results. Further, because they involve safety risks for

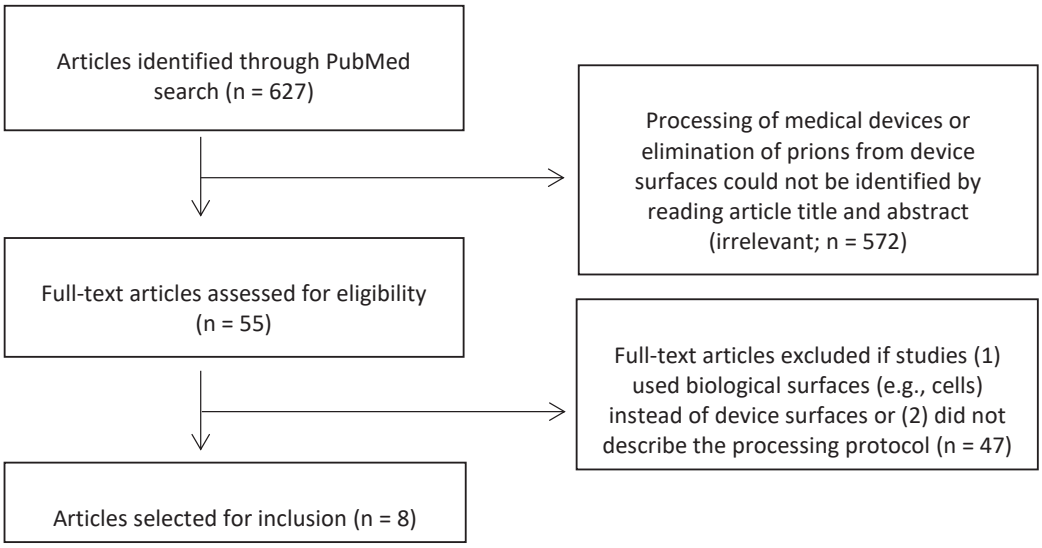

Figure 1. Flowchart of the literature search.

Article (Reference No.)	Surface	Inoculum	Decontamination	Outcome
Secker et al. (26)	New diamond-like carbon tokens doped with Si (2.3%, 5.4%, and 7.8%), N (1.8%, 5.0%, and 8.1%), Fe (1.9%), and TiN	1 µL ME7-infected 10% (w/v) brain homogenate from C57BL/6J mice	Enzymatic precleaning for 5 min, followed by three washes in filtered deionized water. The cleaning solutions tested were Enzol (Johnson & Johnson), Endozime AW+ (Ruhof), Klenzyme (Steris), and Enzycare 2 (Steris)	Reduced protein and prion amyloid contamination was observed on the modified surfaces, and subsequent decontamination efficacy improved.
McDonnell et al. (11)	316L stainless steel wires (5 × 0.16 mm)	10% w/v BH from 263K scrapie strain–infected hamsters	Prolystica 2× enzymatic (0.4%, 50°C), 15 and 30 min; Hamo-100 (0.8%, 43°C), 7.5 min; Hamo-100 (0.4%, 55°C), 5 min; Hamo-100 (0.2%, 55°C), 5 min; ProKlenz-One (0.8%, 25°C), 10 min; Prolystica 10× alkaline (0.16%, 65°C), 2 min; Prolystica 10× alkaline (0.08%, 65°C), 5 min; Prolystica 2× alkaline (0.4%, 65°C), 5 min; Valsure alkaline (2.4%, 65°C), 5 min; disinfection at 90°C, 2 min; steam sterilization at 134°C, 4 min; steam sterilization at 134°C, 18 min; V Pro 1 half-cycle (lumen cycle); V Pro 1 (nonlumen cycle); NaOH 1N, 1 h; 2.5% NaOCl, 1 h; 0.15 mmol/L NaOH, 1 h, 25°C	Traditional chemical methods of surface decontamination against prions were confirmed effective, but the extended steam sterilization method showed variable effects. Thermal disinfection had no impact in these studies. Cleaning with certain defined formulations in combination with steam sterilization was an effective prion decontamination process, particularly with alkaline formulations. Low-temperature, gaseous hydrogen peroxide sterilization was also confirmed to reduce infectivity in the presence and absence of cleaning.
Berberidou et al. (27)	Stainless steel and titanium wires (5.0 × 0.25 mm)	10% w/v BH from 263K scrapie strain–infected Golden Syrian hamsters	224 µg mL^{-1} Fe3+, 500 µg mL^{-1} h^{-1} H_2O_2, UV-A	All Golden Syrian hamsters survived after 480 min of treatment.
Bellon et al. (21)	Stainless steel 316L wires (5 × 0.15 mm and 3 × 0.15 mm)	Infectious BHs (20% w/v in 5% glucose) prepared with brain specimens collected at the terminal phase of disease from 263K scrapie strain–infected Syrian hamsters	NaOH (0.1, 0.15, 0.2, 0.45 mol/L)	Industrial NaOH decontamination regimens attained substantial prion inactivation and/or removal between batches.
Secker et al. (28)	Surgical 316L grade stainless steel tokens (10 × 30 mm)	1 µL ME7-infected 10% (w/v) BH from C57BL/6J mice	Infected tokens were left to dry for 15, 30, 60, 120, or 1,440 min in air, dry polythene bags, or humidity-retention bags. The cleaning solutions tested were Prolystica 2×, alkaline detergent (Steris) and Progenica (Serchem).	Humidity retention bags kept both protein and prion-associated amyloid contamination minimal across the drying times (both pre- and postcleaning).
Hughson et al. (20)	Sterile stainless steel suture wire (3–4 mm)	BHs (10^{-3} to 10^{-10}) from 263K scrapie strain–infected hamsters	A weakly acidic aqueous formulation of HOCl (BrioHOCl), bleach (2.4%), 1N NaOH, and 2% Environ LpH (Steris)	All chemicals were effective in eliminating prions.

Article (Reference No.)	Surface	Inoculum	Decontamination	Outcome
Belondrade et al. (22)	Stainless steel wires (0.15 × 3 mm)	Transgenic mouse brains (tg338 line) infected with 10% 127S prion strain	Water (60 min), peracetic acid 1.2% (60 min), NaOH 0.1N (15 min), NaOCl 0.2% (15 min), NaOH 1N (60 min), NaOCl 2% (60 min), sodium dodecyl sulfate 0.2%/NaOH 0.3% (10 min), steam sterilization (121°C, 20 min), steam sterilization (134°C, 20 min)	Using the protein misfolding cyclic amplification method, the disinfectants below were efficient in eliminating prions: NaOCl (0.2%, 15 min), NaOH (1N, 60 min), NaOCl (2%, 60 min), steam sterilization (134°C, 20 min), sodium dodecyl sulfate (0.2%, 10 min)/ NaOH (0.3%, 10 min).
Nakano et al. (19)	Stainless steel wires (0 and 2 mm)	2 µL of 10% BH with CJD in phosphate-buffered saline	Wires were prewashed in potable water for 1 min, then treated with electrolyzed alkaline water while being sonicated at 45 kHz for 3 min (procedure 1) or 6 min (procedure 2). Then, the wires were rinsed in water with sonication for 1 min and treated with electrolyzed acidic water for 3 min (procedure 1) or 6 min (procedure 2), followed by a rinse with potable water for 1 min. The solution for decontamination was electrolyzed 0.15% NaCl (pH 2.7 and 11.9)	All mice from the wire + BH + wash group survived and remained healthy during the observation period of 600 days after implantation. Five of eight mice implanted with wires + BH, were contaminated with prions.

Table 1. Description of the articles selected in the literature review, including type of surface, inoculum, decontamination method, and outcomes. Abbreviations used: BH, brain homogenate; CJD, Creutzfeldt-Jakob disease; Fe, iron; H_2O_2, hydrogen peroxide; HOCl, hypochlorous acid; N, nitrogen; NaCl, sodium chloride; NaOCl, sodium hypochlorite; NaOH 1N, sodium hydroxide; Si, silicon; TiN, titanium nitride; w/v, weight/volume; UV-A, ultraviolet A.

SPD staff, complicated processes should not be considered for implementation.

Considering that prions can resist steam sterilization processes (thermostability)[15,16] and prions' affinity for binding with metals, developing the cleaning phase of processing for thermoresistant and thermosensitive medical devices is critical. However, only one study has evaluated the cleaning phase adequately and showed positive results with the application of alkaline detergents, which are used by SPDs.[11] Older studies demonstrated up to 99% reduction of organic and inorganic residues through the manual or automated cleaning of medical devices.[17,18] Presoaking and ultrasonic cleaners are recommended for use by SPDs,[12] but their ability to eliminate prions has not been evaluated.

Studies that have proposed introducing new equipment and alkaline, acid, or chlorine solutions in SPDs[19,20] should consider the development of adequate standard operating procedures (SOPs) and management of solutions (i.e., storage and disposal) and equipment (i.e., qualification and validation), which require activity indicators and involve increases in costs and staff training. Also, processing time must be taken into consideration when proposing a processing protocol, in order to ensure viable practices.

The use of 1 nmol sodium hydroxide (NaOH) effectively eliminated prions from surgical instruments.[21,22] However, additional safety precautions need to be implemented in the SPD regarding use of NaOH, which could lead to irreparable damage of surgical

instruments.[14] Studies described the incidence of spills, corrosion, and, in one case, an explosion in the autoclave when 1 nmol NaOH was used.[13]

Various strains of TSEs were used (scrapie, ME7, 263K, and CJD), thereby reflecting the absence of standardized methods to investigate prion contamination. The lack of standardized methods also is a constraint to comparing results, as both prion strains and prion-contaminated devices can differ in several aspects.[10,23] Therefore, standardizing processing methods for medical devices, equipment qualification protocols, cleaning validation protocols, and protocols for monitoring cleaning methods is important.

Identifying prion-positive patients before surgical instruments are reused also is vitally important,[22] especially because rapid assays that can detect prions in surgical instruments are unavailable in clinical settings. Until they become available, protein detection assays are viable alternatives for use in SPDs,[24] though definitive evidence of the absence of protein and risk of prion transmission will remain absent.

Currently, a biopsy is not indicated for diagnosing patients for prion disease[25]; therefore, each healthcare facility should determine the practical situations when the SPD could receive a prion-contaminated surgical instrument. We cannot determine the exact situations when a patient with progressive dementia would undergo a surgical procedure, but an SOP still needs to be prepared in consideration of asymptomatic patients.

Another finding from the current review was the use of low-complexity samples (e.g., wires, tokens) that do not represent the complex instruments used in surgical practice, especially neurosurgeries. For cleaning instruments that contain lumens or dead ends and run on electric power, special protocols and SOPs that include these features will be required.

The application of innovative coatings[26,27] appears promising; however, in addition to being expensive alternatives, these coatings do not solve the problems associated with instruments currently used in SPDs. Moreover, these types of metal-coated instruments are not available for use in SPDs as of yet. Although keeping instruments moist[28] is an inexpensive and easy alternative to reducing prion adsorption, biofilm formation is a concern.[29,30]

Conclusion

The studies reported in this review did not adequately consider current processing practices when developing cleaning procedures for prion-contaminated surgical instruments. Inconsistencies in processing protocols, lack of standards regarding testing and testing end points, and variable results indicate that detailed research is needed to determine leading practices for cleaning and disinfecting prion-contaminated instruments.

Disclaimer

The views, opinions, and/or findings contained herein are those of the authors and should not be construed to represent a position, policy, or decision of the School of Nursing at the University of São Paulo unless so designated by other documentation.

References

1. Griffith JS. Self-replication and scrapie. *Nature*. 1967;215(5105):1043–4.
2. McKinley MP, Masiarz FR, Prusiner SB. Reversible chemical modification of the scrapie agent. *Science*. 1981;214(4526):1259–61.
3. Collinge J, Clarke AR. A general model of prion strains and their pathogenicity. *Science*. 2007; 318(5852):930–6
4. Center for Disease Control and Prevention. Creutzfeldt-Jakob Disease, Classic (CJD): Occurrence and Transmission. www.cdc.gov/prions/cjd/occurrence-transmission.html. Accessed March 19, 2018.
5. Bernouilli C, Siegfried J, Baumgartner G, et al. Danger of accidental person-to-person transmission of Creutzfeldt-Jakob disease by surgery. *Lancet*. 1977;1(8009):478-9.
6. Gibbs CJ, Asher DM, Kobrine A, et al. Transmission of Creutzfeldt-Jakob disease to a chimpanzee by electrodes contaminated during neurosurgery. *J Neurol Neurosurg Psychiatry*. 1994;57(6):757–8.
7. Hachimi KH, Chaunu MP, Cervenakova L, et al. Putative neurosurgical transmission of Creutzfeldt-Jakob disease with analysis of donor

and recipient: agent strains. *C R Acad Sci III*. 1997;320(4):319–28.

8. Nevin S, McMenemey WH, Berhman S, Jones DP. Subacute spongiform encephalopathy: a subacute form of encephalopathy attributable to vascular dysfunction (spongiform cerebral atrophy). *Brain*. 1960;83:519–64.

9. World Health Organization. *WHO infection control guidelines for transmissible spongiform encephalopathies*. www.who.int/csr/resources/publications/bse/WHO_CDS_CSR_APH_2000_3/en. Accessed March 19, 2018.

10. Rutala WA, Weber DJ. Guideline for disinfection and sterilization of prion-contaminated medical instruments. *Infect Control Hosp Epidemiol*. 2010;31(2):107–17.

11. McDonnell G, Dehen C, Perrin A, et al. Cleaning, disinfection and sterilization of surface prion contamination. *J Hosp Infect*. 2013;85(4):268–73.

12. Association of periOperative Registered Nurses. *Guidelines for Perioperative Practice*. Denver, CO: Association of periOperative Registered Nurses; 2016.

13. World Health Organization. *Manual for surveillance of human transmissible spongiform encephalopathies including variant Creutzfeldt-Jakob disease*. http://apps.who.int/iris/handle/10665/42656. Accessed March 19, 2018.

14. McDonnell G, Burke P. The challenge of prion decontamination. *Clin Infect Dis*. 2003;36(9):1152–4.

15. Fernie K, Hamilton S, Somerville RA. Limited efficacy of steam sterilization to inactivate vCJD infectivity. *J Hosp Infect*. 2012;80(1):46–51.

16. Krüger S. Testing cleaning efficacy in decontamination equipment: part 1. *Zentralsterilisation*. 1997;5:333–44.

17. Verjat D, Prognon P, Darbor JC. Fluorescence-assay on traces of protein on re-usable medical devices: cleaning efficiency. *Int J Pharm*. 1999;179(2):267–71.

18. Alfa MJ, Nemes R. Manual versus automated methods for cleaning reusable accessory devices used for minimally invasive surgical procedures. *J Hosp Infect*. 2004;58(1):50–8.

19. Nakano Y, Akamatsu N, Mori T, et al. Sequential washing with electrolyzed alkaline and acidic water effectively removes pathogens from metal surfaces. *PLoS One*. 2016;11:e0156058.

20. Hughson AG, Race B, Kraus A, et al. Inactivation of prions and amyloid seeds with hypochlorous acid. *PLoS Pathog*. 2016;12:e1005914.

21. Bellon A, Comoy E, Simoneau S, et al. Decontamination of prions in a plasma product manufacturing environment. *Transfusion*. 2014;54(4):1028–36.

22. Belondrade M, Nicot S, Béringue V, et al. Rapid and highly sensitive detection of variant Creutzfeldt-Jakob disease abnormal prion protein on steel surfaces by protein misfolding cyclic amplification: application to prion decontamination studies. *PLoS One*. 2016;11:e0146833.

23. Solforosi L, Milani M, Mancini N, et al. A closer look at prion strains: characterization and important implications. *Prion*. 2013;7(2):99–108.

24. UK Department of Health. *Health Technical Memorandum 01-01: Management and decontamination of surgical instruments (medical devices) used in acute care*. www.gov.uk/government/uploads/system/uploads/attachment_data/file/545863/HTM0101PartC.pdf. Accessed March 19, 2018.

25. Center for Disease Control and Prevention. Creutzfeldt-Jakob Disease, Classic (CJD): Diagnostic Criteria. www.cdc.gov/prions/cjd/diagnostic-criteria.html. Accessed March 19, 2018.

26. Secker TJ, Hervé R, Zhao Q, et al. Doped diamond-like carbon coatings for surgical instruments reduce protein and prion-amyloid biofouling and improve subsequent cleaning. *Biofouling*. 2012;28(6):563–9.

27. Berberidou C, Xanthopoulos K, Paspaltsis I, et al. Homogenous photocatalytic decontamination of prion infected stainless steel and titanium surfaces. *Prion*. 2013;7(6):488–95.

28. Secker TJ, Pinchin HE, Hervé RC, Keevil CW. Efficacy of humidity retention bags for the reduced adsorption and improved cleaning of tissue proteins including prion-associated amyloid to surgical stainless steel surfaces. *Biofouling*. 2015;31(6):535–41.

29. Alfa MJ, Sitter DL. In-hospital evaluation of contamination of duodenoscopes: a quantitative assessment of the effect of drying. *J Hosp Infect*. 1991;19(12):89–98.

30. Singh H, Duerksen DR, Schultz G, et al. Impact of cleaning monitoring combined with channel purge storage on elimination of *Escherichia coli* and environmental bacteria from duodenoscopes. Gastrointest Endosc. 2018;88(2):292–302.