Prions are a class of proposed proteinaceous infectious agents that cause similar fatal brain diseases. These diseases are known as transmissible spongiform encephalopathies (TSEs), and include Creutzfeldt-Jakob disease (CJD) and Gerstmann-Straussler syndrome (GSS) in humans, bovine spongiform encephalopathy (BSE) in cattle (also variant CJD [vCJD] in humans), and scrapie in sheep. Iatrogenic transmission of these diseases via contaminated medical devices is considered rare, but it has been documented. In an experimental case, transmission of the disease was observed despite cleaning and decontamination of the medical device with formaldehyde [1]. Clinically, 2 cases of TSEs have been confirmed in which transmission of the disease was due to the use of implanted depth electrodes that had been previously used on a patient with CJD and were inadequately decontaminated by cleaning with benzene and disinfecting with 70% alcohol and formaldehyde [2]. Other cases have been linked to the use of neurosurgical instruments [3]. These reports highlight the need for safe and effective prion decontamination methods.

Recommended prion decontamination practices and methods tend to vary from country to country. For example, in the United States, draft recommendations for medical device disinfection and sterilization have only recently been published [4] and deserve further debate. In contrast, significant controls have been in place for blood collection in the United States for a number of years. This is despite the fact that no known clinical cases of bloodborne transmission of these diseases have been observed and that only recent evidence has shown transfusion transmission in animal models, although even then at a very low level [5]. When one considers that the average number of new cases of CJD, for example, is 1 per 1,000,000 patients, then it is clear that controls for preventing the transmission of the disease in these cases should be in place to reduce the risk of further iatrogenic infections. The emergence of vCJD has further highlighted this need in Europe. Recent guidelines have been published not only in the United Kingdom, but also in several other European countries [6, 7, 8].

Guidelines generally outline 4 major practices for reducing the risk of infection: (1) establishment and documentation of a hospital policy, (2) identification of risk groups and tracking of these patients, (3) use of disposable devices and/or device incineration, and (4) decontamination methods for devices used on at-risk patients. It is clear that every hospital should have a policy in place to deal with potential or confirmed cases of TSEs. Generally, the first step in such a policy is to identify at-risk patients. In most cases, this group consists of patients who receive a clinical diagnosis of or are suspected of having a TSE [9], but it can be expanded to include patients with a known genetic predisposition to TSEs and recipients of types of tissue (including dura mater and pituitary hormones) that have a high risk of being infective. The difficulty with this approach lies in the fact that most of these diseases are generally not recognized until disease symptoms have progressed, as well as in the fact that the majority of cases (85% of CJD cases, for example [3]) are sporadic. Furthermore, as our knowledge of these diseases expands, we need to be aware of the various tissues that can present risks of infectivity. It is widely accepted that tissues such as brain, spinal cord and optic nerve tissue present the highest level of infectivity, but the presence of prions in other tissues has been observed. The presence of the prion protein in other tissues is believed to vary depending on the type and stage of the disease. For example, a recent study on the tissue distribution of the vCJD prion protein reported detecting it in the retina, spleen, and lymph nodes but also found lower concentrations in the rectum, blood, thymus, and adrenal gland [10]. The minimum infectious dose required for disease transmission is currently unknown.

Published guidelines strongly recommend the use of single-use, disposable instruments. For example, despite the low risk of infection, the European Society of
Figure 1. Neurosurgical instruments following treatment by immersion in 1M NaOH and steam sterilization (gravity cycle) at 121°C for 30 minutes

Gastrointestinal Endoscopy recently recommended the use of disposable accessories during endoscopic procedures [11]. It is also recommended that these devices be incinerated after they are removed from circulation. It is intriguing to note that prions have been shown to retain infectivity even following incineration or after being subjected to high autoclave temperatures [12, 13].

Prions are regarded as being highly resistant to the routine methods of decontamination and sterilization that are currently accepted for medical device reprocessing [13]. No single method has been shown to be 100% effective against prions. Therefore, a combination of methods has been recommended, including thorough cleaning, chemical treatment, and/or steam sterilization [9, 14]. Although cleaning is probably the most important step, there are currently no guidelines on which products are more or less effective. It is unknown if currently available cleaners could reduce or increase the infectivity of prions. For example, prions are known to be resistant to enzymes, but enzymatic cleaners do enhance the physical removal of soil from a device. Conversely, cleaners could potentially increase the risk of prion cross-contamination or transmission. Cleaners that contain aldehydes, which are thought to reduce the infectious risks of handling devices, are of particular concern because of their cross-linking mode of action and should not be used for decontamination and sterilization. Further, it is currently unknown what the environmental fate of prion proteins is, which could be a concern if a washer-disinfector is used to clean a contaminated device.

The decontamination methods that have shown significant activity against prions include extended steam sterilization in conjunction with 1M sodium hypochlorite or sodium hypochlorite (2% available chlorine). However, reports on the effectiveness of these methods vary considerably. For example, higher steam sterilization temperatures have actually been suggested to be less effective than lower temperatures [15]. There is good evidence to suggest that the most effective method for prion decontamination involves autoclaving in the presence of high concentrations of sodium hydroxide [13]; however, the safety and physical damage risks associated with use of this method in a hospital environment are of some concern. A hospital in Canada recently attempted to use this method. In this instance, special room ventilation was installed and additional safety precautions were established. Despite this effort, staff complained of obnoxious fumes and found that their devices were extensively damaged and unusable following the process (figure 1; H. Farrow, personal communication). The material compatibility effects—seen and unseen—of these methods on the medical devices may add further risks for patients and should be investigated by manufacturers. In addition, these methods could damage the integrity of the autoclave. More importantly, the safety risks associated with the handling of cold or hot hydroxide and the production of noxious fumes during the processing cycle are significant. Even if chemical treatment is conducted separately from autoclaving, care should be taken to rinse the device prior to autoclaving and to ensure that the autoclave is capable of tolerating higher recommended temperatures (up to 136°C). The safety risks associated with these procedures...
should be considered during the development of a hospital policy.

On the basis of a review of the literature, it is difficult to conclude which sterilization methods are effective, as reports vary considerably. Variability in results may be due to a number of factors. A variety of prion proteins (e.g., the agents of scrapie, BSE, and CJD) have been used, with some suggestion that scrapie strains may be less resistant to sterilization than others, although this remains to be confirmed. Furthermore, a variety of preparation methods (with use of purified or unpurified specimens, homogenates or intact brain) and test methods (e.g., suspension or carrier tests) have been employed. It is well known that the antimicrobial effects of biocides and physical/biocidal processes will vary considerably on the basis of the processing parameters (e.g., active concentration and temperature) and, in the case of liquid chemicals, the formulation effects. Not all of these factors have been considered in the evaluation of prion decontamination methods. A recent example of these effects with use of peracetic acid has been described. Previous testing with peracetic acid was conducted with the biocide alone (in the absence of any liquid formulation) and was shown to be ineffective [16]; however, more recent reports indicate that peracetic acid in a liquid formulation has shown promising activity against prions, though this requires further confirmation [17]. At the same time, use of certain active agents should be contraindicated; in particular, biocides that can potentially cross-link proteins (including formaldehyde, glutaraldehyde, and ortho-phthalaldehyde) should not be used to decontaminate prion-infected materials or devices.

There is clearly a need not only for safe and compatible decontamination methods, but also for consistency in the methodology used to confirm the effectiveness of existing and developing decontamination technologies. It is clear that in vitro methods are currently not sensitive enough for this purpose [1], although reports indicate that protein amplification methods may bring us closer to this goal [18]. In the meantime, in vivo assays are the only alternative. It is important that these methods should be clinically representative and designed to address worst-case scenarios. For example, such a method could be designed on the basis of simulative carrier tests that have shown the ineffectiveness of formaldehyde decontamination, despite previous cleaning [1]. Further validation of this method could be conducted to ensure the safety and reproducibility of existing prion decontamination methods and those being developed.

In conclusion, it is clear that TSE infection control guidelines will continue to evolve. For example, the need for device tracking in hospitals has been under discussion. This issue poses a significant challenge because in many cases the identification of a TSE case may be confirmed only after a surgical procedure. These guidelines and hospital policies should be flexible enough to allow ongoing interpretation of the research on tissue infectivity, detection, infectious risks, and decontamination methods.

References