Creutzfeldt-Jakob Disease: Decontamination Issues

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ABSTRACT

Creutzfeldt-Jakob disease (CJD) is an infectious, progressive, degenerative, neurological disorder with a presumably long incubation period. Once symptoms appear, the disease progresses rapidly from dementia to death. There is no known treatment, and the disease is always fatal. The causative agent, a prion, is extremely hardy and resistant to all measures of decontamination and sterilization routinely used in health care facilities[1] and can live for long periods of time in a dried state.[2] Clearly, CJD poses one of the greatest challenges in decontamination today.

This article outlines precautions to limit the amount of contamination and appropriately decontaminate the operating room and surgical instruments, including the use of barriers, incineration, extended steam sterilization, and chemical disinfection. These precautions should be used for any patient with known or suspected CJD or Gerstmann-Straussler-Scheinker disease (GSS); recipients of human growth hormone, gonadotropin, or human dura mater grafts; and members of recognized familial CJD or GSS families.

BACKGROUND

CJD was first identified in the 1920s by two German psychiatrists for whom the disease was named.[1] The symptoms vary with the area of the brain involved and initially may include confusion and memory loss, impaired gait, vertigo, and visual disturbances.[3] Eventually, the steady progression of symptoms leads the individual to seek medical attention. The electroencephalogram is usually abnormal, demonstrating periodic sharp waveforms. A computerized tomography (CT) scan may show cortical atrophy or enlarged ventricles. Definitive diagnosis is made by a brain biopsy obtained surgically or on postmortem examination. The infected brain tissue contains vacuoles, which give the tissue a spongelike appearance microscopically. For this reason, CJD and related disorders are called transmissible spongiform encephalopathies.[1]

AGENT

The organism causing CJD is smaller than a virus and, unlike other organisms, it can cause an infection without an inflammatory response. The organism is theorized to contain only protein, no DNA or RNA, and replicates by converting normal cellular protein to an aberrant protein. Because these organisms are proteineaceous and infectious, the term "prion" (pronounced pree-on) has been coined to describe them.[4] Other human diseases caused by prions include kuru, GSS, fatal familial insomnia, and familial atypical dementia. Animal prion diseases include scrapie in sheep, chronic wasting disease in elk and deer, transmissible mink encephalopathy, feline spongiform encephalopathy in cats, and bovine spongiform encephalopathy (BSE) in cows ("Mad Cow Disease").[4]

FORMS OF CJD

Three forms of CJD have been described: a) genetic, b) infectious, and c) sporadic.[4,5] Five percent to 15% of cases are thought to be familial, caused by a mutation of the gene encoding the cellular protein on the 20th chromosome.[5] This mutation has been postulated to cause the cellular proteins to mimic and convert to the prion protein and accumulate over time. Mutations have been identified for all affected families with clinical and histologic evidence of CJD.[6]

The second form of CJD is infectious. In this form, the prion protein is introduced from an external source, either orally, parenterally, or implanted surgically. It is theorized that once introduced, the prion protein serves as a template, initiating a series of autocatalytic chain reactions converting cellular protein to the aberrant prion protein.[5] Even with this form of CJD, there appears to be a genetic factor, homozygosity at condon 129, which increases the susceptibility to the infection.[6]

Sporadic CJD accounts for the majority of cases of the disease. This form of CJD is postulated to result from either mutations arising spontaneously in tissue and accumulating over time, or from infectious transmission from an unknown source.[5]

TRANSMISSION

The natural transmission of CJD is not understood, primarily because of difficulties determining causality after a long incubation period. The disease is not transmitted easily, as evidenced by a low incidence rate worldwide (less than one case per million people per year).[1,4] Skin and most body secretions and excretions (eg, urine, feces, milk, saliva, semen) are considered noninfectious.[7] Therefore, social relationships and conjugal living do not pose an increased risk of transmission.[7,8] Reported transmissions have involved direct inoculation of the exposed individual in health care.[1,7,8] Iatrogenic transmissions have occurred via: a) transplanted tissue, b) cadaver-extracted hormones, and c) surgical instruments (*Table 1*).

Transplanted tissue, including cornea, pericardial homograft, and dura mater, has transmitted the disease to recipients.[1,7,8] This mode of transmission is very efficient, directly introducing large quantities of the organism into the central nervous system. The first reported case involved a 55-year-old woman who developed symptoms 18 months after a corneal transplant and CJD was later confirmed.[9] Dura mater grafts have been the source of at least 12 transmissions of CJD.[8,10] When contaminated dural grafts have been implanted during neurosurgical procedures, the incubation period has ranged from 16 months to 9 years.[10] In 1987, precautions were implemented to reduce the risk of transmission via dura mater, including screening of potential donors and more stringent chemical treatment of grafts.[11]

CJD has also been transmitted to at least 51 individuals by subcutaneous injections of human gonadotropin and human growth hormone used to treat dwarfism and short stature.[12] The pool of pituitary glands used to supply the hormones was contaminated by donors with CJD. The resulting doses of the infectious agent were very small, resulting in incubation periods ranging from 2 to 35 years after the last injection. Since 1985, human growth hormone has been manufactured by recombinant DNA techniques, thus eliminating the risk of CJD transmission by this hormone.[7]

Table 1

SOURCES OF REPORTED TRANSMISSIONS OF CJD IN HEALTH CARE

Corneal transplant
Dura mater graft
Pericardial homograft
Human gonadotropin
Human growth hormone
Neurosurgical instruments
Depth electrodes

Recently, a 57-year-old woman developed CJD 2 years after a liver transplant.[13] The donor had no history of neurological disease. In addition to receiving multiple blood transfusions, this patient received albumin derived from blood contaminated with CJD. This case raises questions about a possible transmission from the transplanted organ, blood transfusion, or blood-derived products. In 1995 alone, at least five donors of blood and plasma were diagnosed with CJD and reported to the Food and Drug Administration (FDA).[14] However, the ability to transmit CJD via blood transfusions is only speculative and remains unproven.[7] Based on recommendations by the FDA, the American Red Cross and blood centers have now implemented pre-donation questioning to screen for individuals at high risk for CJD.[14] Also based on FDA recommendations, products derived from blood or plasma from donors later diagnosed with CJD or from recipients of cadaver-extracted hormones or dura mater have been the subject of frequent voluntary recalls since 1994.

CJD has also been transmitted via contaminated surgical instruments. Two

young patients developed CJD after undergoing neurosurgery with depth electrodes.[2] The electrodes had been previously used on a patient with progressive dementia, subsequently diagnosed with CJD. The electrodes were cleaned with benzene, disinfected with 70% alcohol, and placed in a presterilized container with a formaldehyde generator for 2 months prior to reuse on a 23-year-old patient with epilepsy. The decontamination procedure was repeated and the electrodes again used on a 17-year-old patient. These patients developed CJD 20 months and 16 months after surgery. After the last use, the electrodes were decontaminated using the same protocol, placed in the formaldehyde vapor for 2 years, then sent to the National Institutes of Health and implanted into the brain of a chimpanzee. Eighteen months after implantation, the animal displayed evidence of CJD, which was confirmed on autopsy. Contaminated neurosurgical instruments have been implicated in other transmissions of CJD despite decontamination and sterilization techniques.[8] The possibility of contaminated instruments as a mode of transmission is also supported by a case control study that identified intraocular testing with a tonometer; injury or surgery on the head, face, or neck; and trauma to other parts of the body as risk factors for contracting CJD.[15]

Recently, a new variant of CJD unique to Great Britain was identified. The 10 infected individuals were unusually young (16 to 39 years) when symptoms developed and their electroencephalograms were not typical for CJD.[16] This raises the possibility that the cases are linked with a recent epidemic of BSE in that country, either through ingestion of contaminated meat, contact with infected animals, or exposure to an environmental vector. Support for this hypothesis is evident. First, the oral route of transmission is well established for other prion diseases, including kuru, scrapie, and transmissible mink encephalopathy.[17] CJD has been transmitted experimentally to chimpanzees by ingestion of contaminated organs.[17] Dietary sources of meat, as well as animal contact, have also been identified as a risk factor for CJD.[18] Further support is evident from the recent increase in CJD cases in Great Britain, particularly among dairy farmers.[19] In 1989, measures were taken in that country to control BSE, which has been hypothesized to be transmitted to cows by feeding them the remains of sheep infected with scrapie.[19,20]

ERADICATION

Infection control for CJD involves eradication of the CJD agent in health care settings. However, selection of appropriate methods is difficult because of the limitations of the available research. Studies have primarily used different strains of scrapie as a prototype. However, BSE and CJD have also been used.[21-23] These prions have varying levels of infectivity and may not pose the same challenge for eradication.[22] The efficacy of sterilization has been tested using varying amounts of intact brain tissue; dried, macerated brain tissue; and brain homogenates.[21-23] Therefore, it is difficult to compare results between studies. The amount of tissue used in these studies exceeds the amount of bioburden normally found on surgical instruments, making application of findings in health care problematic.

Table 2

INEFFECTIVE OR UNRELIABLE METHODS OF ERADICATION OF PRIONS*

Alcohol
Boiling
Detergents
Dry heat
Ethylene oxide
Formaldehyde
Formalin
Glutaraldehyde
Hydrogen peroxide
Iodophors
Ionizing or ultraviolet radiation
Peracetic acid
Phenolics
Steam sterilization, standard gravity

* Based primarily on work using the scrapie agent.

Recognizing these limitations, it is evident that the repertoire of chemical and physical means routinely used in health care settings does not accomplish adequate decontamination for CJD (*Table 2*). Immersion in glutaraldehyde for 3 weeks is only partially effective. Ethylene oxide is only partially effective after 4 hours of exposure. Formaldehyde renders the organism virtually indestructible, even when subjected to ashing (dry heat at 360°C for 1 hour). Standard gravity sterilization at 121°C for up to 120 minutes is unreliable, as is dry heat at 160°C for 24 hours. Hydrogen peroxide and peracetic acid also do not eradicate prions.[1,7,22]

Incineration destroys prions and is consistently recommended as the method of choice whenever possible.[1,7,24] Steam sterilization in a prevacuum sterilizer for 18 minutes at 134°C produced inconsis-

tent results in controlled experiments. This method was effective against CJD in one study; yet, residual infectivity was present when larger amounts of dried tissue infected with scrapie and BSE were used.[20,21] No cross-contamination in research laboratories has resulted from this method, and it is currently recommended in Great Britain.[20] Standard gravity sterilization at 132°C for 60 minutes effectively eradicated CJD and scrapie infectivity in intact brain tissue.[21] Great Britain's Department of Health (DOH) and the American Neurological Association (ANA) recommend this method.[7,24]

The effectiveness of chemical treatment with sodium hypochlorite has been inconsistent. A 2.5% concentration (25,000 ppm available chlorine) was partially effective against CJD and scrapie.[21] In a recent, more thorough examination of the effectiveness of the chemical, concentrations as low at 8,250 ppm available chlorine for 30 minutes resulted in no residual infectivity.[20] Great Britain's DOH advocates the use of sodium hypochlorite with 20,000 ppm available chlorine for environmental surfaces, with the caveat that the chemical is extremely corrosive to metal. Impervious, disposable table coverings should be used where contamination is expected.[7]

Inconsistent results were found in residual prion infectivity after contact with sodium hydroxide.[20,21] Because no residual infectivity was discovered after exposing small amounts of CJD and scrapie-infected brain tissue to 1M (molar) sodium hydroxide for 60 minutes, the ANA recommends this method.[21,24] More recently, British researchers studied residual infectivity using larger quantities of dried, macerated brain tissue contaminated with BSE and scrapie agents exposed to 1M and 2M sodium hydroxide.[20] Residual infectivity was present in the scrapie-infected tissue after 2 hours. A concentration of 2M is recommended in Great Britain.[7] Sodium hydroxide is less corrosive than hypochlorite and provides a practical means of decontaminating environmental surfaces.[1,21,24] A Japanese study found that the use of a combination of sodium hydroxide (1M) for 60 minutes and standard gravity, low-temperature (121°C) steam sterilization for 30 minutes eliminates residual infectivity of the CJD agent.

Each method of prion eradication discussed poses significant disadvantages:

- Some institutions have limited access to an incinerator.
- Extended high-temperature sterilization damages heat-sensitive surgical instruments.
- Sodium hypochlorite is caustic and significantly damages metal instruments and operating room equipment. Furthermore, the chlorine fumes irritate the respiratory tract.
- Sodium hydroxide is less caustic than hypochlorite, but is a hazardous substance and requires neutralization prior to disposal.
- The combination of hydroxide followed by steam sterilization destroys the finish on metal instruments, rendering them unusable.

Prudent measures of eradicating the organism in an operating room include incineration and prolonged high-temperature steam sterilization. Incineration effectively destroys prions and is the treatment of choice for all contaminated disposable items, sharps, and liquid waste.[1,7] Extended steam sterilization is recommended for reusable instruments, including: a) prevacuum sterilization higher than 134°C for 18 minutes, or b) standard gravity sterilization higher than 132°C for 60 minutes. Use of heat-sensitive items requiring sterilization should be avoided. Impervious, disposable drapes that can be incinerated after use should cover all surfaces where contamination is expected. Environmental surfaces do not require complete sterilization. Therefore, 1M sodium hydroxide for 60 minutes is recommended for decontamination of these surfaces followed by routine cleaning.[1]

DECONTAMINATION

A patient suspected of having CJD or other prion disease may undergo surgical procedures such as a brain biopsy to determine the cause of dementia. The decontamination of the operating room and surgical instruments is usually completed prior to obtaining the definitive diagnosis. Therefore, the precautions described here should be used for any patient at high risk for a prion disease, including: a) any patient with known or suspected CJD or GSS; b) recipients of human growth hormone or gonadotropin; c) recipients of human dura mater grafts; and d) members of recognized familial CJD or GSS families.[7]

PLANNING

Careful planning in advance of the surgical procedure makes decontamination afterwards a manageable task. To the extent possible, use disposable items (eg, drapes, gowns, positioning aids). Because ethylene oxide is ineffective against prions, instruments requiring this method of sterilization should not be used. Likewise, do not use instruments requiring hydrogen peroxide gas plasma or

peracetic acid. Suction tips and needles with small lumens, which are difficult to clean, should be disposable. Powered surgical instruments should not be used for several reasons: a) splattering may lead to an exposure, b) the time required to sterilize the item is unknown, and c) the instrument will be damaged by prolonged steam sterilization. Because detergents have little effect on prions, no items requiring laundry should be used. Remove all unnecessary equipment and supplies prior to the procedure. Tables and equipment near the surgical site (eg, headrest) should be covered with impervious drapes, with edges cuffed for easy removal.

Table 3

PROTECTIVE ATTIRE FOR DECONTAMINATION OF CJD

- Fluid-repellent disposable gown
- Heavy-duty latex gloves (or double latex surgical gloves)
- Surgical mask
- Face shield (disposable)
- Surgical hood/hat
- Shoe covers
- For chemical contact: goggles, chemical-resistant gloves (eg, nitrile)

Table 4

ENVIRONMENTAL DECONTAMINATION

- Use disposable supplies when possible.
- Cover surfaces with impervious drapes when contamination is expected.
- Keep contamination to a minimum.
- Contain, solidify, incinerate liquid waste.
- Contain, incinerate sharps.
- Incinerate all other disposable items.
- Remove contamination with a disposable cloth.
- Apply 1M sodium hydroxide* for 1 hour, then clean with detergent germicide.

*Sodium hydroxide is a hazardous substance and requires precautions.

Table 5

DECONTAMINATION OF SURGICAL INSTRUMENTS

- Open box locks and jaws.
- Wipe instruments with disposable cloth.
- Place in sterilization container.
- Sterilize 18 minutes prevacuum at 135°C or 60 minutes standard gravity at 135°C.
- Verify sterilization parameters.
- Wash in washer/decontaminator.
- Package and sterilize for reuse.

PERSONAL PROTECTION

Care should be taken to avoid personal exposure. The routine protective attire worn for decontamination is appropriate for CJD (*Table 3*). Although prions are not naturally airborne, scrapie has been transmitted through conjunctiva instillation.[25] Therefore, avoid splattering, which may lead to mucous-membrane exposure. Because the route of known transmissions has been direct inoculation, care must be taken to prevent sharps injuries, including avoiding hand-to-hand passing or excessive handling of sharps. Because prions are very small, select durable gloves that provide an adequate barrier during in-use conditions. Vinyl gloves do not give adequate barrier protection.[26] When using strong chemicals, wear chemical-resistant gloves (eg, nitrile) and goggles. Protective attire should be disposable, contained, and incinerated after use.

ENVIRONMENT

Management of CJD in the operating room consists of: a) minimizing equipment and supplies, b) limiting contamination, and c) decontamination postoperatively (*Table 4*). Keep the amount of contamination in the operating room to a minimum. Using two circulators is advised. One circulator controls the contamination while the other performs clean tasks (eg, documentation, accessing cupboards). Caution must be used when removing drapes from the patient, tables, and positioning aids to avoid contaminating the underlying surfaces. When drapes remain intact and are carefully removed, routine cleaning of the equipment (eg, table) with a detergent germicide is adequate. For areas contaminated with blood or cerebrospinal fluid, (eg, floor), use a moist, disposable towel to remove the fluid, and apply 1M sodium hydroxide to the area and leave in place for 1 hour (*Table 4*). Contain, solidify, and incinerate any liquids. This practice eliminates introducing the organism into the sewer system. All disposable items are contained and incinerated, eliminating contamination of a landfill. After 1 hour of contact time with sodium hydroxide, clean the room as per routine with a detergent germicide.

SURGICAL INSTRUMENTS

Specific measures must be taken to prevent transmission of CJD by surgical instruments (*Table 5*). At the end of the procedure, wipe off soiled instruments with a moist, disposable cloth, removing

visible blood and tissue. Using a cloth moistened with water instead of a brush prevents splattering. The instruments should not be submerged in a basin of liquid for several reasons: a) blindly placing hands into a basin of potentially sharp items may lead to a percutaneous exposure, b) splattering may lead to a mucous-membrane exposure, and c) liquid waste requires special treatment prior to disposal. Because the combination of bleach or sodium hydroxide followed by steam sterilization will render stainless-steel instruments unusable, avoid using chemicals for this cleaning. Once free of blood, place instruments, with jaws and box locks open, into the basket of a metal sterilization container. Then put the basket into the sterilization container along with a chemical indicator, seal and sterilize for 18 minutes on a prevacuum cycle at 135°C. Prevacuum is the preferred method. However, a gravity cycle for 60 minutes at 135°C may be used. This temperature allows for a small amount of anticipated fluctuation in the cycle and is routinely used with most sterilizers. Exercise caution to ensure that the container is appropriate for gravity sterilization. The decision whether the container is sterilized in an operating room or decontamination area depends on: a) where the instruments are contaminated, b) the design of the respective areas, c) access to and types of sterilizers available, and d) expertise of staff.

Prior to removal of the container from the sterilizer, the sterilization parameters should be verified and documentation maintained for future reference. Remove the instrument basket from the sterilization container. At this point, prions should be destroyed. However, the instruments are not clean enough for use and will have baked-on debris. The basket of instruments should be processed in a washer/decontaminator using a cycle with a long prewash and washing phase for heavily soiled items. Upon completion of this cycle, the instruments are ready for packaging and sterilization for reuse.

For surgical instruments that cannot tolerate prolonged steam sterilization, a less desirable alternative is immersion for 2 hours in 1M sodium hydroxide. Exercise caution when handling this solution to prevent alkaline burns. Thoroughly rinse instruments following chemical contact and process in a washer/decontaminator as described above. Because sodium hydroxide is a hazardous substance, it must be neutralized prior to disposal in the sewer system.

SUMMARY

CJD poses a unique challenge for decontamination. The organism is especially resistant to cleaning, sterilization, and disinfection procedures routinely used in health care settings. The outlined precautions include the use of barriers, incineration, extended steam sterilization, and chemical disinfection. These precautions should be used for any patient with known or suspected CJD or GSS; recipients of human growth hormone, gonadotropin, or human dura mater grafts; and members of recognized familial CJD or GSS families. ▲

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