01.37 - Transmissible Spongiform Encephalopathies (TSE) including Creutzfeldt - Jakob Disease (CJD)

Purpose To protect healthcare workers from TSE (also known as Prion disease)

Audience All employees of UTMB hospitals, clinics, contract workers, volunteers, and students

At Risk Patients

The following patients are considered to be at risk for TSE:

- Patients with rapidly progressive dementia, ataxia, and myoclonus.
- Patients who have received cadaver-derived hormones, especially growth hormones before 1970.

Healthcare Epidemiology should be notified about all patients considered at high risk for TSE.

Table 2 **Distribution of Infectivity in the human body[1]**

Infectivity Category	Tissues, Secretions, and Excretions
High Infectivity	Brain Spinal Cord Eye
Low Infectivity	CSF Kidney Liver Lung Lymph nodes/spleen Placenta
No Detectable Infectivity	Adipose tissue Adrenal gland Blood Feces Gingival tissue Heart muscle Intestine Milk Nasal mucous Peripheral nerve Prostate Skeletal muscle Testis Thyroid gland Tears Saliva Semen Serous exudate Sweat Urine

[1] Assignment of different organs and tissues to categories of *high* and *low infectivity* is chiefly based upon the frequency with which infectivity has been detectable, rather than upon quantitative assays of the level of infectivity, for which data are incomplete. Experimental data include primates inoculated with tissues from human cases of CJD but have been supplemented in some categories by data obtained from naturally occurring animal TSEs. Actual infectivity titers in the various human tissues other than the brain are extremely limited, but data from experimentally infected animals generally corroborate the grouping shown in the table.

Standard Precautions

Isolation of a patient with TSE is not necessary. Universal Precautions will be used. No special precautions are required for feeding utensils, feeding tubes, suction tubes, or bed linens. All supplies may be disposed of according to routine patient care policy.

Diagnostic Procedures

Except for lumbar puncture, no special precautions are necessary for routine diagnostic examinations (ophthalmoscopic exams, endoscopy, vascular or urinary catheterization, cardiac or pulmonary function tests, etc.). During lumbar puncture, extra care should be taken to avoid spilling CSF on environmental surfaces. Care should be taken to avoid contamination of the outside of the tubes used to collect CSF. All materials used for lumbar puncture including needles should be collected in a puncture-resistant container and sent for incineration.

Surgical Procedures

- Patients who have TSE or are considered at risk for TSE may undergo surgical procedures. Those instruments used for invasive procedures on TSE patients (i.e., used on high or low infectivity tissues) should be securely contained in a robust, leak-proof container labeled “Biohazard”. They should be transferred to the central sterile supply department as soon as possible after use and treated by a method listed in Appendix A.
- Although brain biopsy is not recommended for the diagnosis of TSE, if brain biopsy is performed, the disposable brain biopsy kit will be used, or reusable instruments may be quarantined pending diagnosis. Items for quarantine should be cleaned by the best non-destructive method (see Appendix A), packed, dated and labeled “Hazard” and then stored in specially marked rigid sealed containers. Monitoring and ensuring maintenance of the quarantine is essential to avoid accidental re-introduction of these instruments into the circulating instrument pool. If the TSE is excluded as a diagnosis, the instruments may be returned to circulation after appropriate sterilization. If brain biopsy is performed on a patient with suspected TSE, manual rather than electric saws or drills should be used to minimize the generation of an aerosol of tissue particles and fluids.
- Procedures which are normally carried out at the bedside (LP, bone marrow biopsy) may be performed at the bedside, but care should be taken to ensure ease of environmental decontamination should a spillage occur.

Anesthesia

TSE is not transmissible through the respiratory route. However, instruments in direct contact with mouth, pharynx, tonsils and respiratory tract, should be treated by a method described in Appendix A. Destruction by incineration of non re-usable equipment is recommended.

Childbirth

Childbirth should be managed using standard infection control procedures except that precautions should be taken to reduce the risk of exposure to placenta and associated material and fluids (i.e. use of impermeable gowns, double gloves, mask and goggles or face shield). The placenta should be sealed in a leak-proof container and disposed of by incineration. Instruments should be cleaned and processed by a method in Appendix A.

Laboratory

- Universal Precautions will be followed.
- No special precautions are needed for handling specimens in clinical laboratories except CSF
- Analysis of CSF should not be performed in automated equipment. Any materials coming in contact with CSF must either be incinerated or decontaminated by one of the methods in Appendix A.

Surgical Pathology

- If specimens of high or low infectivity tissue are to be processed and examined by Surgical Pathology at UTMB, the following procedures must be followed:
  - Samples should be labeled “suspected CJD”
  - Single-use protective clothing items should be worn:
    - Liquid repellent gowns over plastic apron
    - Gloves (cut-resistant gloves are preferred for cutting brain tissue)
    - Mask (level 2 or higher)
    - Visor or goggles
- Use disposable equipment wherever possible.
- All disposable instruments that have been in contact with high infectivity tissues should be clearly identified and disposed of by incineration.
- Use disposable non-permeable material to prevent contamination of the work surface. This covering and all washings, waste material and protective clothing should be destroyed and disposed of by incineration.
- Fixatives and waste fluids must be decontaminated by a method in the Appendix or absorbed onto materials such as sawdust and disposed of by incineration.

Waste Disposal

TSE infectious healthcare waste applies only to high and low infectivity tissues from persons with confirmed or suspected TSE, or high infectivity tissue from persons with known prior exposure to cornea, dura mater or human growth hormone, and any disposable items that have come into contact with these tissues. All waste that meets this definition should be placed in secure leak-proof containers and disposed of by incineration.

Precautions for Handling the Deceased Patient

Universal Precautions should be observed. The deceased patient should be placed in a sealed body bag prior to moving. If the skull is open or there is CSF leakage, and where sutures do not completely control this leaking, the bag should be lined with materials to absorb any fluid. If the body is to be transported to the morgue, autopsy personnel must be notified of the suspected diagnosis. This should be done in writing, both on the Cause of Death worksheet, and on the outside of the body bag. Autopsy personnel will notify funeral home personnel when the body is released from the morgue. If the body is to be released to the funeral home directly from the floor, nursing staff must notify the funeral home of the suspected diagnosis.

Autopsy

- Three people should be present during the postmortem examination: the pathologist assisted by one technician and one further person to handle and label the specimen containers. Except for training purposes, observers should be prohibited or kept at a minimum.
- Disposable clothing should be worn including surgical cap, gown, apron, double gloves, and a face shield. Armored or cut-resistant gloves are recommended.
- Disposable or dedicated reusable instruments are recommended.
- A manual saw is recommended to avoid the creation of tissue particulates and aerosols.
- Restricted postmortem examinations on TSE cases can be undertaken. If examination is limited to the brain, a plastic sheet with absorbent wadding and raised edges is first placed underneath the head to ensure containment of tissue debris and body fluids (e.g., CSF). The scalp is reflected in the normal way and the cranium is opened. After removal of the brain, replacement of the skullcap and suturing of the skin, the plastic sheet containing all tissue debris and drainage is bagged and sealed and sent for incineration. A full postmortem examination is discouraged.
- Instruments and working surfaces should be decontaminated following one of the procedures in Appendix A.

Histo-Pathological Examinations

- Only persons who have been advised of the potential hazards and trained in the specific methods used for TSE infectious tissues should be permitted to work in laboratories where high infectivity tissues are being processed.
- It is important to note that formalin and glutaraldehyde-fixed TSE tissue retains infectivity for long periods, if not indefinitely. As a result, they should be handled with the same precautions as fresh material and be considered infectious throughout the entire procedure of fixation, embedding, sectioning, staining, and mounting on slides, until or unless treated with formic acid. Treatment with formic acid reduces infectivity to negligible levels. Although exact procedures may vary, formic acid treatment consists of placing small pieces of fixed tissue, no more than 4 to 5 mm thick, in 50 to 100 ml of 95% formic acid for an hour, and then transferring those to fresh formalin for another two days before further processing. The entire procedure is conducted using continuous, gentle agitation.

- All the serial steps involved in bringing the blocks from formalin into paraffin and, after sectioning, bringing the mounted paraffin sections back into aqueous staining solutions, can be carried out manually, or in an automatic processor dedicated to TSE tissues. Similarly, it would be advisable to dedicate a microtome for sectioning non-formic acid treated tissue blocks, as there is no practical way to disinfect the instrument. Formic acid treated sections can be cut on a standard microtome (if possible, using a disposable knife or dedicated blade) and processed as usual. Processing fluid should be decontaminated and debris (such as wax shavings) from section cutting should be contained and disposed of by incineration. Formic acid treated sections tend to be brittle but show good preservation of histological morphology.
- Slides made from sections which have been treated with formic acid can be considered non-infectious. Slides made from sections that have not been treated with formic acid may also be handled without specific precautions, once the cover slip is sealed to the slide and chemically disinfected to ensure external sterility but should be labeled as a hazardous material. These slides, if damaged, should be treated using a method described in Appendix A.
- Containers used for the storage of formalin-fixed tissues should, after secure closing, be cleaned using a method in the Appendix, marked “Hazardous”, and stored separately (e.g., in sealed plastic bags). When tissue is needed, the container can be removed from the bag, set upon a water-resistant disposable mat, and manipulation of the tissue confined to the mat. After the tissue is replaced, the area and the container are cleaned according to a method in Appendix A, and the container put into a new plastic bag for further storage.

Electron Microscopy

- Electron microscopic examination of tissue sections is not indicated for diagnostic purposes and is not recommended except as an investigational research tool. Preparation of specimens for electron microscopy should be performed with the same precautions as for histopathology. Electron microscopy of tissue sections poses negligible risk both to the microscope and the operator due to the very small amount of tissue deposited on a grid.

Occupational Exposure

Although there have been no confirmed cases of occupational transmission of TSE to humans, cases of CJD in healthcare workers have been reported in which a link to occupational exposure is suggested. Therefore, it is prudent to take a precautionary approach. In the context of occupational exposure, the highest potential risk is from exposure to high infectivity tissues through needlestick injuries with inoculation; however, exposure to either high or low infectivity tissues through direct inoculation (e.g. needlesticks, puncture wounds, ‘sharps’ injuries, or contamination of broken skin) must be avoided. Exposure by splashing of the mucous membranes (notably the conjunctiva) or unintentional ingestion may be considered a hypothetical risk and must also be avoided. Healthcare personnel who work with patients with confirmed or suspected TSE’s or with their high or low infectivity tissues, should be appropriately informed about the nature of the hazard, relevant safety

procedures, and the high level of safety which will be provided by the proposed procedures described throughout this document.

Post-Exposure Management

Appropriate counseling should include the fact that no case of human TSE is known to have occurred through an occupational accident or injury. Several strategies to minimize the theoretical risk of infection following accidents have been proposed, but their usefulness is untested and unknown. For the present the following common-sense actions are recommended:

- Contamination of unbroken skin with internal body fluids or tissues: wash with detergent and abundant quantities of warm water (avoid scrubbing), rinse, and dry. Brief exposure (1 minute, to 0.1N NaOH or a 1:10 dilution of bleach) can be considered for maximum safety.

- Needlesticks or lacerations: gently encourage bleeding; wash (avoid scrubbing) with warm soapy water, rinse, dry and cover with a waterproof dressing. Further treatment (e.g., sutures) should be appropriate to the type of injury. Report the injury according to normal procedures for your hospital or healthcare facility/laboratory.

- Splashes into the eye or mouth: irrigate with either saline (eye) or tap water (mouth); report according to normal procedures for your hospital or healthcare facility/laboratory.

- Health and safety guidelines mandate reporting of injuries, and records should be kept no less than 20 years.

References

1. WHO Infection Control Guidelines for Transmissible Spongiform Encephalopathies. Report of a WHO consultation. Geneva, Switzerland; 23-23: March 1999

2. World Health Organization; Department of Communicable Disease Surveillance and Response.

APPENDIX A

Decontamination methods for Transmissible Spongiform Encephalopathies

The safest and most unambiguous method for ensuring that there is no risk of residual infectivity of contaminated instruments and other material is to discard and destroy them by incineration. In some healthcare situations, as described in the guidance, one of the following less effective methods may be preferred. Wherever possible, instruments and other materials subject to re-use should be kept moist between the time of exposure to infectious materials and subsequent decontamination and cleaning. If it can be done safely, removal of adherent particles through mechanical cleaning will enhance the decontamination process.

The following recommendations are based on the best available evidence currently and are listed in order of more to less severe treatments. These recommendations may require revision as new data becomes available. Refer to Appendix B for the effectiveness of disinfectants.

1. Incineration

- Combustion at 1,000°C is considered the most effective method.
- Use for all disposable instruments, materials, and waste.
- Preferred method for all instruments exposed to high infectivity tissues

2. Autoclave/chemical methods for heat-resistant instruments

- Immerse in sodium hydroxide (NaOH)[1] and heat in gravity displacement autoclave at 121°C for 30 min; clean; rinse in water and subject to routine sterilization.
- Immerse in NaOH or sodium hypochlorite[2] for 1 hr; transfer instruments to water; heat in gravity displacement autoclave at 121°C for 1 hr; clean and subject to routine sterilization.
- Immerse in NaOH or sodium hypochlorite for 1 hr; remove and rinse in water, then transfer to open pan and heat in gravity displacement (121°C) or porous load (134°C) autoclave for 1 hr; clean and subject to routine sterilization.
- Immerse in NaOH and boil for 10 min at atmospheric pressure; clean, rinse in water and subject to routine sterilization.
- Immerse in sodium hypochlorite (preferred) or NaOH (alternative) at ambient temperature for 1 hr; clean; rinse in water and subject to routine sterilization.
- Autoclave at 134°C for 18 minutes.[3]

3. Chemical methods for surfaces and heat sensitive instruments

- Flood with 2N NaOH or undiluted sodium hypochlorite; let stand for 1 hr; mop up and rinse with water.
- Where surfaces cannot tolerate NaOH or hypochlorite, thorough cleaning

will remove most infectivity by dilution and some additional benefit may be derived from the use of one or another of the partially effective methods.

4. Autoclave/chemical methods for dry goods

- Small dry goods that can withstand either NaOH or sodium hypochlorite should first be immersed in one or the other solution (as described above) and then heated in a porous load autoclave at ≥ 121° C for 1 hour.
- Bulky dry goods or dry goods of any size that cannot withstand exposure to NaOH or sodium hypochlorite should be heated in a porous load autoclave at 134°C for 1 hr.

5. Notes for autoclaving and chemicals

- **Gravity displacement autoclaves:** Air is displaced by steam through a port in the bottom of the chamber. Gravity displacement autoclaves are designed for general decontamination and sterilization of solutions and instruments.
- **Porous load autoclaves:** Air is exhausted by vacuum and replaced by steam. Porous load autoclaves are optimized for sterilization of clean instruments, gowns, drapes, toweling, and other dry materials required for surgery. They are not suitable for liquid sterilization.
- **Sodium Hydroxide (NaOH, or soda lye):** Be familiar with and observe safety guidelines for working with NaOH. 1 N NaOH is a solution of 40 g NaOH in 1 litre of water. 1 N NaOH readily reacts with CO_2 in the air to form carbonates that neutralize NaOH and diminish its disinfective properties. 10 N NaOH solutions do not absorb CO_2, therefore 1 N NaOH working solutions should be prepared fresh for each use either from solid NaOH pellets, or by dilution of 10N NaOH stock solutions.
- **Sodium hypochlorite (NaOCl solution, or bleach):** Be familiar with and observe safety guidelines for working with sodium hypochlorite. Household or industrial strength bleach is sold at different concentrations in different countries, so that a standard dilution cannot be specified. Efficacy depends upon the concentration of available chlorine and should be 20,000 ppm available chlorine. One common commercial formulation is 5.25% bleach, for which a 1:2.5 dilution (1 part bleach plus 1.5 parts water) yields the desired working solution. Working solutions should be prepared fresh for each use.

6. Cautions regarding hazardous materials

In all cases, hazardous materials guidelines must be consulted.

- **Personnel**
  NaOH is caustic but relatively slow acting at room temperature and can be removed from skin or clothing by thorough rinsing with water. Hot NaOH is aggressively caustic and should not be handled until cool. The hazard posed by hot NaOH explains the need to limit boiling to 10 minutes, the shortest time known to be effective.

  Hypochlorite solutions continuously evolve chlorine and so must be kept tightly sealed and away from light. The amount of chlorine released during

inactivation may be sufficient to create a potential respiratory hazard unless the process is carried out in a well-ventilated or isolated location.

- **Material**

  In principle, NaOH does not corrode stainless steel, but in practice some formulations of stainless steel can be damaged (including some used for surgical instruments). It is advisable to test a sample or consult with the manufacturer before dedicating a large number of instruments to decontamination procedures. NaOH is known to be corrosive to glass and aluminum. Hypochlorite does not corrode glass or aluminum and has also been shown to be an effective sterilizing agent; it is, however, corrosive both to stainless steel and to autoclaves and (unlike NaOH) cannot be used as an instrument bath in the autoclave. If hypochlorite is used to clean or soak an instrument, it must be completely rinsed from the surfaces before autoclaving. Other decontamination methods may need testing, or consultation with the manufacturer to verify their effect on the instrument.

[1] Unless otherwise noted, the recommended concentration is 1N NaOH.
[2] Unless otherwise noted, the recommended concentration is 20 000 ppm available chlorine.
[3] In worse case scenarios (brain tissue bake-dried on to surface) infectivity will be largely but not completely removed.

APPENDIX B

Ineffective or sub-optimal disinfectants		
Chemical disinfectants	**Gaseous disinfectants**	**Physical processes**
Ineffective[17] Alcohol Ammonia B-propiolactone Formalin Hydrochloric acid Hydrogen peroxide Peracetic acid Phenolics Sodium dodecyl sulfate (SDS) (5%)	Ineffective Ethylene oxide formaldehyde	Ineffective Boiling Dry heat (<300˚C) Ionizing, UV or microwave radiation
Variably or partially effective Chlorine dioxide Glutaraldehyde Guanidinium thiocyanate (4M) Iodophores Sodium dichloro-isocyanurate Sodium metaperiodate Urea (6M)		Variably or partially effective Autoclaving at 121˚C for 15 minutes Boiling in 3% sodium dodecyl sulfate (SDS)

[16] Guidelines for the Safe Transport of Infectious Substances and Diagnostic Specimens. Geneva, World Health Organization, 1997. WHO/EMC/97.3.

[17] Some of these chemicals may have very small effects on TSE infectivity and are not adequate for disinfection.