Subject: Prion Disease – Transmissible Spongiform Encephalopathy (CJD etc.)	Original Issue Date: April 2000 Supersedes: March 2018	**Effective Date:** Oct 2021
Departments Consulted: Microbiology Lab Laboratory Services Pathology Department	**Reviewed & Approved By:** Paul Holtom MD, Hospital Epidemiologist Noah Wald-Dickler MD, Associate Hospital Epidemiologist Chair and Vice-Chair, Infection Control Committee	**Approved By**: Brad Spellberg, MD Chief Medical Officer

PURPOSE:
The purpose of this policy is to prevent exposure and/or transmission of suspected or diagnosed prion disease to patients, families, and healthcare personnel.

DEFINITION
Transmissible spongiform encephalopathies (TSE) are progressively fatal diseases of humans and animals caused by prions. Prions are unique infectious agents in that they contain no DNA or RNA and they are resistant to standard sterilization methods. These diseases are classified as transmissible spongiform encephalopathies because of the characteristic spongy degeneration of the brain and their ability to be transmitted to laboratory animals. TSE is characterized by progressive dementia, myoclonus, and often-typical electroencephalogram. The clinical course usually lasts several years and is invariably fatal. Human diseases caused by prions include: Creutzfeldt-Jacob Disease (CJD), Variant CJD, Gertsmann-Sträussler-Scheinker Syndrome (GSS), Kuru, fatal familial insomnia (FFI) and protease-sensitive prionopathy.

I. GENERAL INFORMATION

A. Transmission Risk

Potentially infectious body fluids and tissue carry the greatest risk of transmission during invasive procedures (especially in the operating room and autopsy suite). For routine patient care, no special precautions are required; standard precautions should be followed. The World Health Organization (WHO) categorizes potentially infectious body fluids and tissues into three risk groups. The following list identifies which body fluids and tissues are **potentially infectious:**

Table 1: Distribution of prion infectivity in the human body

INFECTIVITY	SUBSTANCES
High Infectivity Tissues and Fluids	Central Nervous system, specifically: Brain, Spinal Cord, Eye, CSF
Low Infectivity Tissues and Fluids	Kidney, Liver, Lung, Lymph nodes, Spleen, Placenta and Tonsils
No Detectable Infectivity	Blood, other Body Fluids, and tissue such as: Adipose, Adrenal gland, Gingival tissue, Heart muscle, Intestine, Peripheral nerve, Prostate, Skeletal muscle, Testis, Thyroid gland, Tears, Nasal mucous, Saliva, Sweat, Serous exudate, Milk, Semen, Urine, Feces etc.

B. Etiology

Traditional virologic methods have not identified the etiologic agent. The etiologic agent is an unconventional filterable agent (prion). Currently there is no test to detect an immunologic response to infection.

C. Epidemiology

CJD has been identified in all developed countries and is thought to occur worldwide. Incidence of CJD is estimated at about 1 case per million persons per year (range 0.09-31.1) Although most cases are sporadic, familial aggregation has been reported. CJD is not a reportable disease in the United States but must be reported to the Los Angeles County Department of Public Health within 7 calendar days.

D. Modes of Transmission

The exact mode of transmission in humans is not known, however disease can be induced in laboratory animals by percutaneous inoculation of infective material (brain or cerebral spinal fluid), not by simple direct contact. Transmission of CJD has not been associated with environmental contamination or fomites. Transmission has been associated with contact with contaminated tissues, specifically central nervous system tissue and eye. Person-to-person transmission via skin contaminated contact has not been documented. Transmission has been documented by the use of contaminated neurosurgical instruments or use of infected dura mater, cadaveric growth hormone, contaminated corneal transplants, contaminated EEG electrode implants, contaminated dura mater grafts, and receipt of contaminated human growth hormone.

E. Incubation Period

Fifteen months to possibly more than 30 years in the iatrogenic cases. Those with known direct CNS tissue exposures have been associated with incubation periods of less than 10 years. Unknown in sporadic cases, but probably as long as in Kuru (4 to over 20 years).

F. Period of Communicability

CNS tissues are infectious throughout symptomatic illness. Other tissues and CSF are sometimes infectious. Infectivity during the incubation period is not known, but studies in animals suggest that lymphoid and other organs are probably infectious before signs of illness appear.

G. CJD Facts

CJD is a rare neurological disorder caused by prions that's been seen in the United States for decades. This is different from the variant that has been linked to beef consumption in Europe. Little is known about how most CJD cases are acquired, and there are no currently available therapies. The disease has a lengthy incubation period, but once symptoms appear it causes a rapid decline in neurologic function, followed by death.

According to the Centers for Disease Control and Prevention:

- Clinical features include a neurological presentation, with dementia, and a progressive cerebral syndrome including ataxia, gait and speech abnormalities. In most patients these symptoms are followed by involuntary movements and atypical electroencephalogram tracings.
- In more than 85% of the cases, the duration of CJD is less than one year (median 4 months).
- From 10-15% of CJD cases are inherited, but cases have been associated with the use of contaminated corneal transplants, electrode implants, dura mater grafts, and receipt of human growth hormone.
- CJD occurs worldwide at a rate of about 1 case per million population per year.
- From 1979 to 2017 the US annual rate was 3.5 cases per million in persons over 50 years of age.
- The disease is found most frequently in patients 55 to 65 years of age. In the United States CJD deaths among persons under 30 years are rare (fewer than 5 deaths per billion per year).

Source: Centers for Disease Control and Prevention, 2018.

II. ADMISSION PROCEDURES

A. Responsibility

1. **Attending Physician and/or Admitting Physician:**
   It is the responsibility of the attending and/or admitting physician to inform the following departments/people upon admission - or as soon as the diagnosis is being contemplated - that a patient is suspected or confirmed to have prion disease.
   a. Admitting Department/Bed Control
   b. Hospital Epidemiologist
   c. Infection Control Practitioner
   d. Nursing Supervisor
2. Prior to scheduling a patient with suspected or confirmed prion disease for any invasive procedure, ***Infection Control must be notified*.**

III. INVASIVE AND PERIOPERATIVE PROCEDURES

A. Classification of Risk

The following procedures are defined as invasive and "high-risk" for possible prion transmission:
All surgical procedures including:
   a. Brain Biopsy
   b. Stereotactic procedures
   c. Endoscopic procedures
   d. Bronchoscopic procedures

B. General Information

1. Biopsies will not be performed to establish diagnosis of TSE.
2. Disposables will be utilized over non-disposables. All non-disposable instruments utilized during the procedure will be sequestrated until results of genetic/diagnostic testing are completed and forwarded to Infection Control.
3. **Prior to scheduling a patient with suspected or confirmed prion disease for any invasive procedure, Infection Control, the area Charge Nurse, or the Nurse Manager must be notified**.
4. Formic Acid Protocol will be followed during processing of tissue (see Section VII).
5. Frozen section will not be performed.
6. Flash sterilization of contaminated instruments is prohibited.
7. Maintain one-way flow of instruments.
8. Traffic within the operating room or procedure room will be kept to a minimum. Only essential personnel will be present.
9. Environmental Services will wear scrubs with disposable cover gown, double glove, mask and protective eye covering for decontamination/cleaning procedures.

C. Recommendations for All Invasive or Surgical Procedures

1. All invasive OR procedures must be performed in a suite designated by the OR. In emergent situations outside the OR, contact the Infection Control Practitioner at extension x96645.
2. All cases must be scheduled and coordinated with the OR charge nurse. The Infection Control Practitioner will assist the OR Charge Nurse and the OR nursing director with assigning appropriate room.

3. Every attempt will be made to place the case as the last case of the day to allow adequate cleaning and decontamination.
4. Standard Precautions will be followed at all times.
5. Use as few instruments and supplies as possible.
6. Use disposables over non-disposables as much as possible.
7. In-patients where the diagnosis of prion disease is strongly suspected or confirmed, who require endoscopic procedures, a specific reserved scope will be used. This scope will undergo soaking in 1N NaOH for 1 hour after the procedure and will not be placed back into general use for other endoscopic procedures.
8. Exclude all items that cannot be sterilized by either steam autoclaving or soaking in 1N NaOH.
9. Use no power tools, including drills.
10. Limit access to essential OR staff or department staff only.
11. Wear full personal protective apparel (PPE) when performing invasive procedures:
    a. Eye protection
    b. Head covering (caps)
    c. Surgical mask
    d. Shoe covers
    e. Double gloves
    f. Surgical gown

D. Responsibility for Notification

1. **Attending Physician and Surgeon Notifies**:
   It is the responsibility of the attending physician and the scheduling surgeon to inform the OR nursing director or area director (where the procedure is to be performed) and the Infection Control Practitioner that the patient is suspected of having or diagnosed with prion disease. Notification of any invasive procedure must be made as far in advance as possible to allow for purchase of disposable instruments.

2. **Infection Control Notifies**:
   a. Central Supply Manager
   b. Environmental Services Director
   c. Chief of Pathology
   d. Director of Clinical Laboratory

3. **Operating Room/Nursing Director Notifies**:
   The following departments with the date, time and patient information scheduled for the procedure:
   a. OR Nurse Manager or Charge Nurse
   b. Anesthesia Coordinator and Chief of Service
   c. Infection Control Practitioner (responsible for notifying Chairman, Infection Control Committee)
   d. Facilities Management (to adjust autoclave settings to 134°C = 270°F for 1 hour, see Section III E)

4. **Operating Room/Nursing Director will also:**
   a. Allow an additional 2 hours for environmental decontamination
   b. Document "Prion Disease Precautions" on the OR/Department schedule

5. Operating Room or Procedure Room Staff will be augmented for:
   a. One scrub nurse/procedure nurse
   b. One in-room circulating nurse
   c. One staff member stationed outside the operating/procedure room

E. Procedure Room Preparation

1. Prior to patient arrival:

a. Standard Precautions are to be followed at all times.
b. Extraneous furniture, supplies, and equipment will be removed from the room prior to patient arrival.
c. Items that cannot be removed will be withdrawn to the perimeter and covered with disposable drapes.
d. All drawers and cabinets will be closed.
e. All case carts will be positioned outside the operating/procedure room.
f. The operating room/procedure room table mattress will be covered with disposable drapes
g. All staff associated with the case will change to disposable scrubs
h. Open sterile instrument supplies and remove unnecessary instruments
i. Discard any trash and linen.

2. Instrumentation

a. Use only disposable instruments or
b. Use only non-disposable instruments that can withstand prolonged steam sterilization at 134°C for 1 hour (e.g., stainless steel) or non-disposable instruments that can be immersed for 1 hour in 1N NaOH (sodium hydroxide). See Section IV: B.
c. Use of power equipment (e.g., drills) is prohibited.
d. Use only disposable cautery cords.

3. Intra-Operative/Intra-Procedure Activity

a. The staff member stationed outside the room acts as a traffic controller and provides requested equipment or supplies to the room as needed.
b. Only the outside staff member may:
    i. Access closed drawers and cabinets
    ii. Obtain supplies and equipment from outside the room
    iii. Provide requested supplies and equipment from outside the room
c. Only the inside circulator may:
    i. Provide supplies and equipment to the scrub nurse or procedure nurse
    ii. Accept instruments, tissue or other materials handed off the sterile field
d. Attempt will be made to isolate those instruments used from those not used throughout the case.
e. **NO HAND-TO-HAND PASSING OF SHARPS DURING THE CASE/PROCEDURE.**
f. All sharps are to be passed in a sterile emesis basis or pan.
g. All spills of body fluid or tissue will be cleaned with NaOH (sodium hydroxide).
h. Personal Protective Equipment will be worn by all staff at all times during the case and during handling of specimens. PPE will not be removed until the completion of the case and all biohazardous waste is properly disposed of (red bagged, removed from room). Environmental Services will incinerate.

4. Specimen Management

a. Tissue specimen(s) will be passed off the sterile field to the inside circulator.
b. The scrub nurse hands the container off to the inside circulator who applies the required labels.
c. The inside circulator places the specimen inside a clean plastic specimen bag held open by the outside staff member.
d. All specimens will be labeled "R/O Prion Disease".
e. The diagnosis field of the Pathology Request Form will be labeled "R/O Prion Disease".
f. The specimen will then be hand-delivered directly to the pathologist.
g. **Do NOT transport any specimens by pneumatic tube system (to prevent spills and breakage).**
h. CSF cultures will be performed in disposable plates.

i. CSF cell counts: use sterilized Hemocytometer that is committed for use only for CSF that potentially contains prions (CJD, Kuru, variant CJD etc.)
j. CSF chemistries: generally, CSF glucose and protein are of limited utility in the diagnosis of prion disease.
k. Once the specimen test has been completed, the pathologist will have the specimen/tissue/plates incinerated. Call Environmental Services for incineration.

5. Post-Procedure Care of the Patient

a. Prior to leaving the room, contaminated intact skin surfaces will be washed 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.
b. Dressing will be applied with clean gloves.
c. Patient will be recovered in OR/procedure room
d. The outside staff member will assist in transport to patient room.

6. Post-Procedure Staff Responsibility

a. Professional staff and all support (including Environmental Services, Radiology, Lab) will change clothes (scrubs) as soon as possible at the conclusion of the case. Soiled clothing will be bagged and sent to Environmental Services for incineration via red container used for pathological waste.
b. Environmental Services personnel will dispose and incinerate PPE and cleaning cloths via red containers used for pathological waste.

IV. DECONTAMINATION AND CLEANING PROCEDURES

A. General Considerations

TSE prion agents are resistant to disinfection and sterilization by most physical and chemical methods commonly used for decontamination of infectious pathogens. As such, special procedures are required for environmental, instrument and waste decontamination in the setting of suspected or confirmed TSE. Variability in effective decontamination is influenced by the nature and physical state of infected tissues. For example, infectivity is stabilized by drying or fixation with alcohol or formalin. As such, contaminated materials should not be exposed to fixation reagents, and should be kept wet between time of use and disinfection.

B. Use of Hazardous Chemicals: Sodium Hydroxide and Sodium Hypochlorite (Bleach)

Standard decontamination methods may be ineffective in removing prion infectivity, thus requiring the use of hazardous materials, particularly sodium hydroxide (NaOH) and/or sodium hypochlorite (Bleach, NaOCl). Both are caustic to human skin and mucous membranes. Staff will obtain hazardous chemicals, including NaOH and sodium hypochlorite, from pharmacy. Appropriate PPE must be worn at all times while handling these chemicals including: eyewear, masks, gloves, scrub gown.

Sodium Hydroxide: is caustic but relatively slow acting at room temperature and can be removed from skin or clothing by thorough rinsing with water. In principle, NaOH does not corrode stainless steel, but in practice some stainless steel products can be damaged (including some used for surgical instruments). Consult with manufacturer before subjecting a large number of instruments to NaOH decontamination procedures. Unless otherwise noted, the recommended concentration for NaOH is 1N (e.g., 40g NaOH in 1L water).

Sodium Hypochlorite (Bleach): solutions continuously evolve chlorine and so must be kept tightly sealed and away from light. Hypochlorite does not corrode glass or aluminum, but it is corrosive both to stainless steel and autoclaves. So unlike NaOH, bleach cannot be used as an instrument bath in an autoclave. If bleach is used to clean or soak an instrument, it must be completely rinsed from surfaces before autoclaving. Consult with the manufacturer to verify effect on instruments. Bleach is sold at different concentrations, so a standard dilution cannot be specified, but unless otherwise stated, recommended concentration is 20,000 ppm (often 5% bleach).

C. Recommendations for Sterilization and Disinfection

Instruments must undergo a longer sterilization time before further use. Combining two or more different procedures appears to be most effective. Tissues, all surgical instruments and all wound drainage should be considered contaminated and must be inactivated by either sterilization or incineration. The following guidelines for sterilization and decontamination are recommended by the World Health Organization (WHO):

1. Use only disposable surgical instruments; incinerate and dispose of them after use. This is the preferred method for all instruments exposed to high infectivity tissues (see Table 1) and is the safest and most unambiguous method for ensuring no risk of residual infectivity on contaminated instruments. Where disease is not confirmed, instruments may be cleaned and quarantined without use pending diagnostic test.

2. If disposal and incineration are not possible, decontaminate and reprocess materials as follows:

Heat-Resistant Instruments

1. Instruments subject to reuse should be kept moist between the time of exposure to infectious materials and subsequent decontamination/cleaning: placed soiled instruments in an enzymatic detergent as soon as possible after use.

2. Follow with thorough mechanical cleaning (prior to sterilization) to remove adherent particles and reduce the bio-burden.

3. After thorough mechanical cleaning, immerse instruments in sodium hypochlorite (bleach) or sodium hydroxide (NaOH) at ambient temperature for 1 hour; remove and clean; rinse in water and subject to routine sterilization as below in Table 2.

Heat-Sensitive Instruments

1. Flood with 2N (not 1N) NaOH or undiluted sodium hypochlorite (bleach); let stand for 1 hour; mop up and rinse with water.

2. When surfaces cannot tolerate NaOH or undiluted sodium hypochlorite, thorough cleaning will remove most infectivity by dilution. Added benefit may be derived from use of another method.

Table 2: Recommended Temperatures for Sterilization			
Type of Sterilizer	**Recommended Temperature**	**Sterilization Cycle Duration**	**Type of Materials Sterilized**
Pre-Vacuum Steam Sterilization (Porous Load Autoclave) Cycle	135°C – 138°C	18 minutes	Clean Instruments, Gowns, Drapes, Towels and Dry Materials
Standard Gravity Steam Sterilization Cycle	135°C – 138°C	60 minutes	Clean Instruments and Solutions

***Endoscopic Equipment*:** risk of prion transmission during endoscopies has not been reported.

1. Blood and body fluids encountered during endoscopy are categorized as "Low to No Risk" infectivity
2. **Prior to any endoscopic procedure, Infection Control should be notified** with decisions regarding endoscopy to be made on a case-by-case basis.
3. In patients who require endoscopic procedures, a specific reserved scope will be used. This scope will undergo soaking in 1N NaOH for 1 hour after the procedure and will not be placed back into general use for other endoscopic procedures.
4. The hospital's other current policies and procedures for sterilization endoscopic equipment will be followed.

Dry Goods

1. Small dry goods that can withstand either NaOH or bleach should be immerse in one or the other solution (as above) and then heated in a porous load autoclave at ≥121°C for 1 hour.
2. Bulky dry goods or dry goods that cannot withstand exposure to NaOH or bleach should be heated in a porous load autoclave (Pre-Vacuum Steam Sterilizer) at 134°C for 1 hour.

Linens

1. Use PPE as above including double gloves; strict hand washing is required.
2. Non-invasive procedures: use standard cleaning, regular laundering and routine waste handling.
3. For invasive procedures: place items in leak-proof yellow plastic container and label "For Incineration" or double bag and steam sterilize at 132-134°C for 1 hour then dispose in red biohazardous waste bag. Call Environmental Services to dispose.

D. Post-Procedure Decontamination, Disinfection and Cleaning

1. Surgical Instrumentation
    a. All non-disposable instruments used will be cleaned as soon as possible after use to minimize drying of tissues, blood and body fluids on the items which could increase infectivity.
    b. Avoid mixing instruments used on "No Detectable Infectivity Tissues" with those used on "High Infectivity" and "Low Infectivity Tissues".
    c. The scrub nurse will place all instruments in an instrument basket and then into:
        i. Sterilizer if immediately adjacent
        ii. Covered transport container with lid locked and transported to Central Service Dept
    d. Central Service personnel will pre-soak in an enzymatic detergent prior to decontamination and cleaning.
    e. Follow with thorough mechanical cleaning to remove adherent particles & reduce bio-burden.

f. After thorough mechanical cleaning, immerse in sodium hypochlorite (Bleach) or sodium hydroxide (NaOH) at ambient temperature for 1 hour; clean, rinse in water, and subject to routine sterilization as described in Table 2.
g. Two assigned personnel will verify that all instruments used during the case have been appropriately decontaminated and that required sterilization parameters have been maintained. Sterilizer load numbers and contents will be documented in the steam sterilization log.

2. Procedure Room Instrumentation
   a. The procedure nurse will dispose of all disposable instruments in red, biohazard waste bags.
   b. Non-disposable instruments will be handled in the same manner as surgical instruments (see above).
   c. Environmental Services will dispose of all biohazardous waste by incineration via red barrels.

3. Disposal of Contaminated Fluids
   a. All fluids should be suctioned into impervious disposable containers.
   b. All canisters will be capped and discarded in red biohazardous waste bags.
   c. Environmental Services will dispose of all biohazardous waste by incineration via the red barrels.

4. Disposable Equipment
   a. Environment Services will be notified at the completion of the case.
   b. All disposable material and used linen will be placed in red impervious biohazard bags/containers and designated for incineration by Environmental Services via the red barrels.

5. Exposed Environmental Surfaces
   a. All exposed surfaces and equipment that came into direct contact with tissue or debris from the procedure will be decontaminated with 5% Bleach (sodium hypochlorite).
   b. Surfaces must remain in contact with the bleach for 2 hours.
   c. Surfaces will then be thoroughly rinsed with water and cleaned per routine procedure.

V. ACCIDENTAL EXPOSURE TO CONTAMINATED TISSUE

1. *Percutaneous Exposure* (Needlesticks and Lacerations)
   a. Gently encourage bleeding, wash with warm soapy water (avoid scrubbing), rinse, dry and cover with a waterproof dressing.
   b. Report the exposure incident to Employee Health and Supervisor immediately.
   c. Follow the Post-Exposure Prophylaxis Guidelines Policy and Procedure.
2. *Mucous Membrane Exposure and/or Conjunctival Exposure*: (splashes into eye or mouth)
   a. Flood exposed area with water.
   b. Report the exposure incident to Employee Health and Supervisor immediately.
3. *Contamination of Unbroken Skin with Internal Body Fluids or Tissues*
   a. Wash contaminated intact skin surfaces with detergent and abundant quantities of warm water (avoid scrubbing), rinse, and dry.
   b. Brief exposure (e.g. 1 minute) to 0.1N NaOH or a 1:10 dilution of bleach can be considered.
4. Follow the Bloodborne Pathogen Control Plan/Management of Accidental Exposures.

VI. AUTOPSIES

1. Autopsies will not be performed on-site on a patient known or suspected to have prion disease.
2. If a patient known or suspected to have prion disease requires an autopsy, the case will be referred to the Coroner's Office. Consent for autopsy will only be obtained in coordination with the CDC-supported National Prion Disease Pathology Surveillance Center
   https://case.edu/medicine/pathology/divisions/prion-center

VII. LABORATORY POLICY FOR HANDLING OF TEST REQUESTS

Presently, the only Orchid-orderable test for prion disease is the CSF 14-3-3 protein, although this is not the preferred diagnostic method. When the lab receives a request for a test related to prion disease (including 14-3-3 protein), an alert is triggered so that appropriate personnel and departments are notified. The lab tech will notify the laboratory supervisor who will contact:

1. Core, Microbiology and other pathology labs and Administrative Managers
2. Hospital Epidemiology (x96645 main or x96565 physician VoIP)
3. Pathology Resident on call for Chemistry

The Pathology Resident will be familiar with issues surrounding prion disease and perform the following:

1. Immediately review the Prion Policy in this guideline.
2. Inform the ordering physician that they need to notify epidemiology (x96645), the nurse manager and obtain an Infectious Disease consultation if they have not done so. Notification allows the patient's chart to be flagged with the appropriate identifier/med alert code.
3. Notify Surgical Pathology (x94606 Histology supervisor or designee) and Cytology (x94615 Cytology supervisor or designee). If Surgical Pathology and Cytology are closed, notification should be at the beginning of the next business day. Notification avoids performing frozen sections of contaminated tissue specimens.

Specimen Ordering and Handling for Prion Disease Testing (including CSF 14-3-3)

All testing will be coordinated with and performed at the CDC-Sponsored National Prion Disease Pathology Surveillance Center at Case Western Reserve University (NPDPSC). As of 2015, the NPDPSC will test for prions in CSF using a second generation real-time quaking-induced conversion assay to detect the pathologic prion protein (PrP). This method is more sensitive and specific than older CSF 14-3-3 assays alone. Providers ordering "14-3-3 Protein CSF, T-tau, reflex to RT-QuIC-NonInt" in Orchid will require approval from the on-call physician Hospital Epidemiologist with formal Infectious Disease Consultation to assess clinical appropriateness of testing.

NOTE: all specimens require the ordering physician to complete the appropriate Test Requisition Form which may be found at: https://case.edu/medicine/pathology/divisions/national-prion-disease-pathology-surveillance-center/resources-professionals/testing-protocols.

CSF should be collected by lumbar puncture and frozen as quickly as possible (preferably within 20 minutes) and stored at -80°C (or lacking that, in a -20°C freezer) and shipped in dry ice. CSF will be hand-delivered to lab and labeled "R/O Prion Disease".

Blood is non-diagnostic and should ONLY be used when a familial CJD case is confirmed by family pedigree or when requested by the NPDPSC. If blood is submitted for genetic sequencing for familial prion disease, four purple top (EDTA) tubes each containing 5 mL blood should be collected. Please coordinate with lab as blood should be shipped on the same day it is collected. Tubes should be stored and shipped at room temperature using protective bubble wrap or Styrofoam. If blood is submitted for genetic sequencing without a confirmed, attached family pedigree and clinical history, the referring institution will be charged test costs of $412. For blood genetic testing results to be reported, the appropriate form must be completed which can be found at:
https://case.edu/medicine/pathology/sites/case.edu.pathology/files/2018-06/testing-and-reporting-genetics-consent.pdf For additional questions contact the NPDPSC at 216-368-0587.

Brain Biopsy: will generally not be performed for the diagnosis of prion disease. If rare circumstance requires, freeze 0.5g of grey matter tissue in a -70°C freezer (or lacking that, in a -20°C freezer) and ship in dry ice. 0.5g is ideal, but smaller tissue amounts may be acceptable if no additional tissue is available. Remaining tissue should be fixed in 10% buffered formal for at least 24 hours followed by 1 hour formic acid (range of formic acid between 88-98%) treatment then by at least 24 hours of additional fixation in formalin (the 24 hours includes shipping time). If the formic acid treatment cannot be performed prior to shipping, the NPDPSC may be able to perform it after paraffin embedding on the tissue extracted from the melted paraffin block.

Autopsy: autopsies will not be performed on-site. These cases will be referred to the Coroner's Office. Obtain consent for autopsy of brain only in coordination with the NPDPSC. Consent must include signed Authorization for Post-Mortem Examination Form available at:
https://case.edu/medicine/pathology/sites/case.edu.pathology/files/2019-12/NPDPSC%20Autopsy%20Consent.pdf

REFERENCES

1. CDC 2018. Prion Disease. https://www.cdc.gov/prions/index.html
2. WHO 1999. Infection Control Guidelines for Transmissible Spongiform Encephalopathies in Humans. https://www.who.int/csr/resources/publications/bse/WHO_CDS_CSR_APH_2000_3/en/
3. Belay E, Schonberger L. The Public Health Impact of Prion Diseas. *Annu Rev Pub Health* 2005;26:191-192.
4. Baldwin KJ, Correll CM. Prion Disease. *Semin Neurol*. 2019;39(4):428-439.