Human Prion Disease Policy

POLICY 4.2
Patient Care
Title of Policy
Issued: 04/1989
Last Approval: 12/2025

I. PURPOSE

A. To prevent transmission of Human Prion Diseases (HPDs) from patients with HPD to other patients or healthcare personnel. Prion diseases constitute a unique infection control problem because prions exhibit unusual resistance to conventional cleaning, disinfection, and sterilization methods.

II. REFERENCES

A. "Creutzfeldt-Jakob Disease, Classic (CJD)." Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 10 Sept. 2021, https://www.cdc.gov/prions/cjd/index.html.

B. Rutala, W.A., et al., Creutzfeldt-Jakob Disease: Guidelines for Disinfection and Sterilization of Prion-Contaminated Medical Instruments. Infection Control and Hospital Epidemiology 2010 Feb;31(2):107-17

C. "WHO Guidelines on Tissue Infectivity Distribution in Transmissible Spongiform Encephalopathies." World Health Organization, https://www.who.int/publications/m/item/who-guidelines-on-tissue-infectivity-distribution-in-transmissible-spongiform-encephalopathies.

D. Hazardous Material and Waste Management Plan Policy 3.1.0

E. Clinical Pathology Standard Operating Procedure (SOP) Document #G203

F. Cytology Lab Standard Operating Procedure Document #C316

G. CDPH Emerging Infections Program Reporting Requirements (https://ceip.us/projects/cjd/local-health-departments/)

III. DEFINITIONS

A. **Human Prion Diseases (HPDs):** Neurodegenerative diseases that are caused by protein-based infectious agents called prions, also known as transmissible spongiform encephalopathies (TSE). Examples include sporadic and familial Creutzfeldt-Jakob disease (CJD), variant CJD (vCJD), Gertsmann-Straussler-Scheinker disease (GSS), and fatal familial insomnia (FFI).

B. **High-risk Criteria for Human Prion Diseases:**

1. Patients with known or suspected prion diseases

2. Rapidly progressive dementia consistent with prion diseases with ongoing diagnostic workup

3. Patients undergoing brain biopsy when a specific lesion has not been demonstrated (e.g., on MRI or CT)

4. Familial history of CJD, GSS, or FFI

5. Patients known to carry a mutation in the PrP gene involved in familial transmissible spongiform encephalopathies (TSEs)

6. Patients who have had healthcare-associated exposure to HPD (e.g., receipt of dura mater graft, human gonadotropin, corneal transplant, or pituitary-derived nonrecombinant human growth hormone derived from persons with HPD).

C. **Infectivity categories for tissues:**

1. **High-infectivity**: Brain, spinal cord or eye tissues from suspected/confirmed human prion disease (HPD) patients that pose highest risk of containing transmissible prion proteins.

2. **Low-Infectivity**: Cerebrospinal fluid, kidney, liver, lung, lymph nodes/spleen, placenta tissues from suspected/confirmed HPD patients that pose low risk of containing transmissible prion proteins

3. **No Infectivity**: All other tissues (not listed above) from suspected/confirmed HPD patients that pose no risk of transmission of prion proteins. Such tissues/secretions/excretions include adipose tissue, gingival tissue, heart muscle, intestine, peripheral nerve, skeletal muscle, blood, saliva, sweat, breast milk, semen, urine and feces.

D. **Spaulding classification for reusable medical devices/instruments:**

1. **Critical**: Instruments that enter sterile tissue, body cavities, or the vascular system (e.g., surgical instruments, implants)

2. **Semi-critical**: Instruments that contact non-intact skin or mucous membranes (e.g., bronchoscopes).

3. **Noncritical**: Instruments that contact only with intact skin.

IV. POLICY

A. All UCSF Medical Center personnel are required to adhere to these procedures to prevent transmission of prions from patients with suspected/confirmed HPD to personnel or other patients.

V. PROCEDURES

A. Any confirmed case of human prion disease diagnosed by a neurologist or confirmed by CSF testing or tissue pathology must be reported:

1. Immediately to UCSF Hospital Epidemiology and Infection Prevention (HEIP)

2. Within seven days of diagnosis to the local public health department where the patient resides (e.g., San Francisco Department of Public Health) using the Confidential Morbidity Report (CMR) form. See submission details on the SFDPH website.

3. If available, hospital discharge summaries, neurology notes, MRI and EEG reports, CSF and brain biopsy/autopsy lab results, and a copy of the death certificate should be attached to the CMR form.

B. Routine care of patients with suspected or confirmed HPD

1. Adhere to Standard Precautions when caring for any patient, including patients with suspected or confirmed HPD.

2. A private room is not required for patients with suspected or confirmed HPD.

3. Handle patient waste in accordance with Hazardous Material and Waste Management Plan Policy 3.1.0

4. Use routine practices that minimize splashing to dispose of liquid body substances such as blood, urine, bile, vomitus, stool or other secretions/excretions, and dispose of them in the sanitary sewer (toilet, hopper, or lab sink).

5. Handle feeding utensils, feeding tubes, suction tubes, items used in skin or wound care, and bed linens using routine hospital practices.

C. Bedside lumbar punctures on patients with suspected or confirmed HPD

1. Obtain a Human Prion Disease Lumbar Puncture Kit (also called CJD LP Kit) and request a pathologic/medical waste bin from Hospitality services. The Human Prion Disease Lumbar Puncture Kit contains:

   a. Disposable lumbar puncture tray
   b. Long sleeve fluid-resistant disposable gowns
   c. Masks with eye protection
   d. Door Sign: “Do Not Enter! Procedure in Progress”
   e. Sharps container
   f. Occlusive dressing material to cover LP site
   g. Red medical waste bags
   h. Fluid-resistant drapes
   i. CJD (HPD) lab specimen labels

2. Obtain a biohazard-marked lab specimen bag and place a CJD lab specimen label on the bag

3. Minimize exposure by ensuring that the patient is alone in the room and/or roommate is absent

4. Cover surfaces around the patient (bed, linen, table) with disposable impermeable drapes and line the waste barrel with a red medical waste bag.

5. Place a sharps container near procedure area.

6. Set up the sterile field in the standard fashion.

7. Any healthcare provider involved in the lumbar puncture must wear a long sleeve fluid-repellant, disposable gown, gloves, mask and eye protection.

   a. The provider performing the lumbar puncture will wear double sterile gloves; all others should wear one pair of gloves.

8. Transport specimens to the Clinical Laboratory with the appropriate labels and documentation:

   a. Ensure that CSF specimen tubes are labeled with the patient's name and the CJD lab specimen label.

   b. Place CSF specimen tubes in biohazard-marked lab specimen bags and affix a CJD lab specimen label on the outside of each bag.

   c. Verbally communicate with the lab personnel receiving the specimen that "CJD/HPD" precautions are necessary.

   d. Document where the specimen will be delivered and who will be transporting the specimen in the patient's medical record.

9. Post-procedure waste: Please refer to section VII for instructions on waste disposal

10. Post-procedure room cleaning: Please refer to section VI for instructions on cleaning and disinfection of environmental surfaces.

D. Imaging and interventional radiology-guided lumbar puncture:

1. Imaging-guided lumbar puncture. Follow all steps described under "C. Bedside lumbar puncture"

   a. Schedule these procedures to allow time for appropriate room set up and post-procedure cleaning.

   b. The attending interventional radiologist will ensure that the supplies listed in section V.C.1 are available before initiation of the procedure.

   c. For procedures requiring anesthesia, see Section V.E.7: Anesthesia, below.

d. After the procedure, the table and radiologic equipment will be cleaned by the radiology technologist in accordance with the recommended procedure for cleaning as described under section VI. “Cleaning and disinfection of contaminated environmental surfaces”.

2. Other radiology procedures that require anesthesia

a. Anesthesia instruments used for intubation or sedation are considered semi-critical instruments that are in contact with tissues where there is no risk of transmission (no infectivity tissues) and can therefore be routinely reprocessed as per the manufacturers’ instructions for use.

E. Surgery: The following sections pertain to surgeries involving high-infectivity tissues (e.g. brain, retina, dura matter, trigeminal ganglia, optic nerves, spinal cord, pituitary glands, spinal ganglia) performed on patients with suspected or confirmed HPD. Of note, testing for HPD is most commonly based on tests performed on CSF specimens. Brain biopsy for HPD diagnosis is no longer frequently performed, but in the event that a patient has an undetermined neurological condition in which HPD is being considered as a possible diagnosis that has not yet been ruled out, the following precautions should be followed.

1. Preoperative:

a. The attending or resident surgeon booking a case must communicate suspected or confirmed Human Prion Disease status to the operating room scheduling coordinator and pod manager for neurosurgery.

i. If a diagnosis is not documented in the scheduling system, the scheduling coordinator will contact the surgeon and ask if HPD is being considered as a possible diagnosis.

ii. For example, if a burr hole procedure is booked for 'Brain Biopsy: other' (i.e., not for tumor), then the Neurosurgery service must confirm that CJD or another HPD is not a clinical consideration.

b. The pod manager will notify HEIP of the suspected or confirmed HPD patient scheduled for high infectivity tissue surgery to receive additional preparation guidance.

c. Scheduling:

i. Cases should be scheduled early in the day to allow adequate time for cleaning and processing of specimens in surgical pathology.

ii. The scheduling coordinator or the OR front desk staff will notify the Neurosurgery pod manager of the surgical case.

iii. Neurosurgery Pod manager will notify the following as far ahead of time as possible.

(a) PACU Assistant Nursing Director

(b) OR Charge Nurse

(c) SPD Director

(d) Instrument Coordinator/Lead Tech

(e) OR support supervisor

(f) On-call Hospital Epidemiology and Infection Prevention (HEIP) infection preventionist via Voalte

(g) Pathology

(h) Environmental Health and Safety – request white Human Prion disease waste tub

2. Operating room preparation

a. The circulating nurse will request a dedicated CJD kit with consumable and disposable instruments from Material Services. This kit includes:

i. Copy of this policy

ii. Red medical waste bags for incineration

iii. Sterile gloves

iv. Sterile surgical gowns

v. Eye protection

vi. Shoe covers

vii. Disposable BP cuffs (both pediatric and adult)

viii. Isolation sign

ix. Tags and notification forms for EH&S

b. OR hampers and kick buckets will be lined with red medical waste bags

c. The attending surgeon will determine the unit location where the patient will be sent post-operatively and the unit will be notified in advance.

d. The circulating nurse will place the appropriate signage on the OR doors and remove all non-essential equipment from the room.

e. The OR table and table padding will be covered by a fluid-impervious sterile drape to prevent any high-risk tissue/fluid from contaminating the OR table and pads.

3. Surgery: Intraoperative

a. In addition to PPE required for routine surgical procedures, the scrub team will wear:

i. Double gloves

ii. Eye protection

b. All other personnel entering the OR should use PPE consistent with the standard OR policy.

4. Surgical instruments: All surgical instruments that could come into contact with high-infectivity tissues should be disposable, if possible. For all neurosurgical procedures:

   a. Request a disposable external ventricular drain (EVD) instrument set from Material Services

   b. Anticipated intraoperative use of any non-disposable instruments that could come into contact with high infectivity tissues must be discussed with SPD prior to the start of the procedure.

   c. See Section VI "Handling and reprocessing of surgical or procedural reusable instruments"

5. Handling of surgical specimens

   a. The circulating RN will invert the specimen bag to cover their hand while the scrub nurse passes the specimen.

   b. The circulator will invert the bag over the cup once the specimen is obtained.

   c. All specimens will be bagged and labeled with a "CJD lab specimen" label

   d. The circulating RN will notify Pathology to pick up the specimen in the OR at the time of surgery and that Human Prion Disease precautions are required. Specimens will be picked up immediately by the pathology resident.

6. Surgery: Post-operative

   a. Nurse responsibilities:

      i. All linens used in the Operating Room, including bed sheets, blankets, towels and any disposable materials exposed to high-infectivity fluids/tissues, must be placed in red medical waste bags. These bags must be placed in the medical waste bins for pick up by Hospitality for incineration.

         (a) Any linens that are not exposed to high-infectivity tissues/fluids in the Operating Room including bed sheets, blankets, and towels, can be handled using routine soiled linen reprocessing.

         (b) Disposable linens that do not come into contact with high-infectivity tissue/fluid can be disposed of according to standard procedure.

7. Anesthesia

   a. Procedures

i. All anesthesia providers should wear personal protective equipment per standard procedure.

ii. Anesthesia equipment:

(a) Can be reprocessed using routine protocols unless contaminated with high-infectivity tissues

(b) Clean and disinfect the anesthesia machine surfaces using routine procedures unless contaminated with high-infectivity tissue. If contaminated with high-infectivity tissue, refer to section VI. Cleaning & Disinfection. Discuss with the Director or the Director of the Sterile Processing Department (SPD) or designee.

F. Clinical Laboratories

2. Clinical pathology:

a. When tissues labeled as "CJD/HPD lab specimens" are received in the Pathology Laboratory, please refer to Clinical Pathology Standard Operating Procedure (SOP) Document #G203 for procedures for handling specimens.

a. If the Gross Pathology Laboratory becomes aware of possible prion disease after the high-infectivity tissue specimens have passed through the laboratory, the pathology supervisor must be notified and will provide instructions for decontamination procedures.

3. Cytology Laboratory:

b. If the cytology laboratory becomes aware of possible prion disease specimens after the specimen has passed through the laboratory, the lab will follow Cytology Lab SOP Document #C316 which provides instructions on decontamination procedures.

VI. Cleaning & Disinfection of Contaminated Environmental Surfaces & Instruments

A. Bedside and Image-Guided Lumbar Puncture

1. Use routine standard room and surface cleaning procedures unless CSF spillage has occurred (see below for additional steps).

2. Hospitality staff will wear disposable fluid-resistant gowns, eye protection, surgical masks, shoe covers (if shoe contamination is anticipated), and heavy-duty gloves for cleaning the room.

3. Pour bleach at a 1:10 dilution (i.e., one part bleach to 10 parts water—this is available as a prediluted liquid product) onto single use cleaning cloths to wipe down all surfaces that have come into contact with CSF, and leave undisturbed for at least 15 minutes.

   a. If Hospitality does not have bleach available and cannot perform the necessary cleaning, contact the Spill Response Team via UCSF Police Department (UCPD) at 415-476-6911 to handle room cleaning and spills.

4. Discard cleaning equipment (i.e. cleaning cloths and mop heads) into red medical waste bags.

5. Complete and affix Hazardous Waste tags to each red bag and discard into medical waste bins marked Human Prion Disease Waste.

6. Hospitality will dispose of medical waste bins for incineration.

B. Cleaning and disinfection of contaminated environment/surfaces in the Operating Room:

1. Personal Protective Equipment -- Staff cleaning the OR will wear:

   a. Disposable fluid-resistant gown

   b. Surgical mask and eye protection

   c. Heavy-duty gloves

   d. Shoe covers

2. Decontaminate all room surfaces that may have come into contact with high-infectivity tissues with bleach at 1:10 dilution including the OR table, instrument tables, and floor at the head of the bed by pouring the 1:10 bleach solution onto single use cloths to soak and wipe those surfaces.

3. If Hospitality does not have bleach available, contact the Spill Response team to perform the OR decontamination.

4. Do not use spray bottles

5. Allow bleach to sit wet and undisturbed for at least 15 minutes

6. After air drying, rinse area thoroughly with water, then clean floor and surrounding area per standard procedure

7. To clean floor:

   a. For contaminated floors, pour 1:10 bleach directly onto floor at the floor level, taking care not to splash. Do not use a mop bucket.

   b. Allow bleach to sit undisturbed for at least 15 minutes before wiping.

8. Decontaminate the remainder of the room according to standard procedure.

C. Handling and reprocessing of reusable surgical instruments

1. Instrument Types:

a. Single-use disposable instruments are recommended for surgical or procedural interventions (e.g. lumbar punctures or brain biopsy) for patients with suspected or confirmed HPD. After use, these instruments are discarded into red bags for incineration.

b. Non-disposable instruments that contact high-infectivity tissues of patients with suspected HPD must be quarantined prior to instrument re-processing while awaiting the results of HPD testing.

c. Staff handling instruments that have come into contact with high-infectivity tissues while under quarantine or during reprocessing must wear:

i. Long sleeve fluid-resistant gown

ii. Surgical mask

iii. Eye protection

iv. Heavy duty water-repellant gloves

2. Instrument quarantine procedure: Follow this procedure if HPD was not suspected preoperatively but intra-operative neuropathologic results suggest possible prion disease, or if HPD is suspected but diagnosis has not yet been confirmed.

a. Immediately contact HEIP, OR Nursing director, SPD Director, Neurosurgery Chief

b. Immediately after use, hand off instruments for quarantine to lead SPD Technician or SPD Supervisor

c. SPD will place instruments into red medical waste bags and label the bags, “Human Prion Disease Quarantine”.

d. Instruments will be brought to the SPD decontamination area.

e. SPD staff will moisten instruments with a hospital-approved pre-cleaner or enzymatic cleaner.(e.g., Ecolab Opto-Pro Gel Pre-cleaner). Prions are hydrophobic and in the absence of moisture will strongly attach to the surface, particularly stainless steel. Ensure instruments are moist at all times. SPD will monitor instruments every hours and reapply approved cleaning agent to keep instruments moist.

f. If the instrument composition and chemical intolerances are unclear, consult the MIFU or contact the manufacturer.

g. Keep moistened instruments in quarantine area designated by the SPD director.

h. Instruments will remain in quarantine until a HPD diagnosis has been either confirmed or ruled out.

i. If a diagnosis of prion disease is confirmed and instruments can receive full steam sterilization, follow the instructions in section VI.C.2.i.

ii. If a diagnosis of prion disease is confirmed but instruments cannot receive full steam sterilization, then place instruments into red medical waste bags for incineration.

iii. If prion disease has been ruled out, then reprocess instruments by using standard reprocessing procedures.

i. Non-disposable, multi-use instruments exposed to high-infectivity tissue that can receive full high-temperature steam sterilization:

i. Instruments with a large amount of bioburden must be either discarded or decontaminated by hand, with the worker wearing full protective gear (see Section VI.C.1.c)

ii. Brushing to remove organic material must be done with the instrument(s) submerged in a hospital-approved enzymatic cleaner. Keeping items below the surface of the solution will minimize spray from the cleaning equipment.

iii. Immediately place instruments in an automated washer-disinfector and clean with 1:10 bleach for 1 hour.

iv. Remove instruments from washer-disinfector and rinse in water.

v. Allow solution in sink to flow down the drain.

vi. Rinse sink and all treated areas thoroughly with water.

vii. Autoclave instruments by one of the two procedures listed:

(a) Autoclave at 134C for 1 hour in a porous load autoclave; or

(b) Autoclave at 121C for 1 hour in a gravity displacement autoclave

viii. After autoclaving is complete, clean and subject instruments to routine sterilization

j. Non-disposable surgical instruments exposed to high-infectivity tissues that cannot be cleaned and/or cannot receive full high-temperature steam sterilization must be clearly labeled for disposal by incineration.

k. Instruments that contact low- or no-infectivity tissues can be reprocessed using standard procedures.

VII. Waste Disposal

A. Handling of waste after bedside lumbar puncture (bedside & imaging-guided)

1. Discard all instruments used for the procedure, any contaminated materials, and the sharps container into the medical waste bins lined with the red medical waste bag.

2. Linens and patient gowns that are contaminated by CSF should also be placed into red medical waste bags in the medical waste bins.

3. Linen that has not been contaminated with CSF during the procedure can be placed in a covered linen container as per routine hospital policy.

4. Contact the primary nurse and/or unit clerk to place an MCSS ticket for hospitality pick up and disposal of waste.

5. If CSF contamination or spill occurs, notify the primary nurse and/or unit clerk to notify Hospitality.

B. Handling of OR waste:

1. All linens used in the Operating Room, including bed sheets, bath blankets, towels, and any other disposable materials in contact with high-infectivity fluids/tissues must be placed in red medical waste bags.

2. Suction all liquid waste into one suction canister then dispose of the canister by double bagging the suction cannister into red medical waste bags and place into the red medical waste bin.

3. Line the medical waste bin with the red medical waste bags.

4. The circulating nurse will complete and affix Hazardous Waste tags to each red bag and discard these into the medical waste bin marked Human Prion Disease Waste Only.

5. Complete one MCSS ticket to Hospitality for all red-bagged items for medical waste pick-up. It is safe to store the properly packaged materials in a secure area until pick-up.

6. Any soiled linen that has not been exposed to high-infectivity tissue/fluids in the operating room including bed sheets, bath blankets, and towels can be placed in regular soiled linen bags for routine processing.

C. Handling and disposal of cleaning equipment used in OR:

1. Double bag all cleaning equipment, e.g., single-use cleaning cloths and mop heads that contact surfaces potentially contaminated with high-infectivity tissues, into red medical waste bags.

2. Place all red medical waste bags in the medical waste bins for Human Prion Disease waste.

3. Complete one MCSS ticket to hospitality, for all red-bagged items. It is safe to store the properly packaged materials in a secure area until pick-up.

D. Handling of waste in the Clinical Pathology Lab

1. Clinical Pathology lab does not perform autopsies or handle high-infectivity tissues from deceased patients with suspected or confirmed HPD.

2. Please refer to Clinical Pathology SOP Documents #G203 and #C316 for details.

VIII. Patient Exposures

A. In the unlikely event that a HPD diagnosis is made after neurosurgical instruments have been routinely reprocessed and used on other patients:

1. Immediately notify HEIP, Risk Management, Regulatory Affairs, Patient Safety, the Chief of Neurosurgery, perioperative leadership, and the Director of SPD.

2. SPD will identify all instruments used during the surgical procedure for the patient with confirmed HPD potentially in contact with high-risk tissues/fluids and immediately sequester these instruments from further use.

3. SPD will identify all patients and procedures where these instruments were used after use on the index HPD patient.

4. HEIP will coordinate a multidisciplinary discussion to assess risks and to provide recommendations regarding the need for patient notifications and will notify public health authorities.

5. Regulatory Affairs and Risk Management will determine the method for patient notifications, if notification is recommended.

IX. Occupational exposures

A. Although there have been no confirmed cases of occupational transmission of HPDs to humans, transmission through contact with high-infectivity tissues is theoretically possible.

B. Possible modes of transmission are from high-infectivity tissues through direct inoculation, such as by:

1. Skin puncture or injection

2. Ingestion

3. Contact with mucous membranes (eyes, nose, mouth)

4. Contact with non-intact skin

C. Employee Responsibilities: First aid and reporting

1. Perform first aid according to the type of exposure/ injury.
    a. First aid for an intact skin exposure:
        i. Wash with soap and abundant quantities of warm water (avoid scrubbing), rinse, and dry.
    b. First aid for splashes to the eyes, nose, or mouth:
        i. Immediately flush the area with running water (mouth) or normal saline (eyes). Continue washing for 15 minutes. Do not rub or keep eyes closed.
    c. Percutaneous injuries (e.g., lacerations or needlestick injuries)
        i. Gently encourage bleeding; wash (avoid scrubbing) with warm soapy water, rinse, dry and cover with a dressing.
        ii. Further treatment (e.g. sutures) should be appropriate to the type of injury.

2. For all exposures, contact the Occupational Health Needlestick Exposure Hotline (415) 353-7842 to report the exposure. The employee will need to follow up with the UCSF Occupational Health Clinic.

3. Inform your supervisor of the exposure and complete an Incident Report.

4. For immediate care for any injury, proceed to the Emergency Department (ED).

D. Employee Responsibilities: Garment disposal and equipment management
    1. Splash affecting garments:
        a. Remove garments that may have become soiled or contaminated with high-infectivity tissue and place them in a red medical waste bag.
        b. Close the bag securely, label it for incineration, and wash hands thoroughly.
        c. Red medical waste bags should be placed in a medical waste bin.
        d. Place an MCSS ticket to hospitality for pick-up of bin for incineration.

    2. Equipment Management:
        a. Identify the mechanism of exposure and place any equipment involved in the exposure (surgical instruments, procedural instruments, etc.) into a red medical waste bag and then into a medical waste bin.
        b. Make sure that the area has been secured and that signage of contamination has been posted to prevent other individuals from entering the area.

E. Emergency Department and Occupational Health Responsibilities
    1. When necessary, treatment of the injury, if needed, should be initiated in the Emergency Department as soon as possible.
    2. The Emergency Department physician should consult with the Needlestick Exposure Hotline for information and advice.
    3. A Doctor's First Report of Injury (DFR) should be completed.

X. RESPONSIBILITY

A. UCSF Hospital Epidemiology & Infection Prevention is responsible for updating this policy.

XI. HISTORY OF POLICY

A. Issued: 4/1989, Revised: 4/01, 9/01, 11/01, 3/02, 5/02, 12/02, 4/04, 10/05, 7/10, 4/12, 5/12, 6/15, 3/16, 3/22, 12/2/25