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Recommendations for Laboratory Handling of Low Risk Specimens, including Cerebrospinal Fluid, from Patients under Investigation for Creutzfeldt-Jakob Disease

As described in the *Canadian Biosafety Guideline: Human Diagnostic Activities*, facilities are encouraged to conduct a local risk assessment (LRA) for diagnostic activities, taking into consideration the potential for infectious aerosol and droplet production and the risk of exposure. This will assist in determining appropriate mitigation measures that reduce site-specific and activity-specific risks. Best practices for conducting an LRA can be found in the *Canadian Biosafety Guideline: Local Risk Assessment*. Facilities are also responsible for compliance with provincial and local legislation on decontamination and waste management.

These recommendations are intended to support LRAs for diagnostic laboratories where only low risk materials are handled (i.e., cerebrospinal fluid [CSF], blood, saliva, urine). The UK Advisory Committee for Dangerous Pathogens (ACDP) Transmissible Spongiform Encephalopathy (TSE) subgroup has revised the laboratory guidelines for handling TSE tissues, which were published on November 18th, 2021 [1]. These guidelines can be used as reference material when performing LRAs for the handling of specimens from patients at risk of CJD.

In addition to these recommendations, facilities may consider referring to the Public Health Agency of Canada's Canadian Biosafety App, which can be used to filter prion-related requirements from the Canadian Biosafety Standard, Third Edition.

Background

Prion diseases, such as Creutzfeldt-Jakob Disease (CJD) in humans, are fatal and transmissible disorders characterized by neurodegeneration. The infectious agent is composed of misfolded forms of prion protein that form insoluble aggregates in the brain. Prions can propagate by templating the misfolding of normal forms of the protein. This process occurs primarily in the brain, spinal cord and some related tissues including cranial nerves and ganglia, the posterior eye and pituitary. People have been infected with prions by medical or surgical procedures involving contaminated neurosurgical tools as well as by injuries that puncture the skin whilst handling high risk materials (e.g., brain tissue) [2]. ***Biofluids and peripheral tissues contain low titres of infectivity*** and therefore present a low risk of exposure to prions [3-5].

Biosafety considerations for diagnostic activities

Various laboratory tests may be required for the investigation of patients with neurodegenerative dementia and suspected CJD. ***Processing of specimens from these patients should not be delayed*** until confirmatory tests for CJD are completed, such that it may unnecessarily delay or compromise patient care.

Notable low risk materials include blood, urine, saliva, CSF, faeces, and most peripheral (i.e., non-central nervous system) tissues. Only general laboratory protective measures are needed when handling these materials; no additional precautions over and above those taken for other CSF, blood, saliva, and urine specimens need to be taken for the analysis, storage, and disposal of these types of specimens from patients with suspected CJD.

General laboratory protective measures for specimens from patients at risk of prion diseases (i.e., those from patients with neurodegenerative conditions including dementia) would include the use of suitable personal

protective equipment (PPE) as determined by an LRA. Examples of recommended PPE include eye protection, liquid-repellent gown or plastic apron, gloves and protective covering of cuts and abrasions. Any contamination of the skin should be washed (not scrubbed) with warm soapy water.

Although we recommend that ***automated laboratory equipment*** used in the processing of CSF samples from patients at risk of prion diseases be decontaminated according to local laboratory guidelines, we note that manufacturers may have specific requirements and a local risk assessment should be performed prior to use.

Various operational precautions could be considered as part of a LRA when considering the handling of CSF specimens from patients at risk of prion diseases. These include:

- undertaking laboratory manipulations in a biological safety cabinet (BSC), separate room, or dedicated area of the laboratory;
- undertaking laboratory manipulations at a predetermined quieter time of the day (e.g., at the beginning or end of the day);
- designating personnel to perform testing of these specimens;
- covering the bench in a spill-resistant covering, or spill tray that can be disposed of or decontaminated by standard local procedures, in case of spills;
- avoiding the use of sharps (e.g., glassware, scalpels);
- using disposable laboratory consumables and equipment where possible;
- decontaminating non-disposable items and equipment after use according to local laboratory guidelines;
- using normal clinical waste to dispose of used laboratory consumables, in accordance with local and provincial legislation.

1. https://www.gov.uk/government/publications/guidance-from-the-acdp-tse-risk-management-subgroup-formerly-tse-working-group
2. Brandel JP, Vlaicu MB, Culeux A, Belondrade M, Bougard D, Grznarova K, Denouel A, Plu I, Bouaziz-Amar E, Seilhean D, Levasseur M, Haïk S. Variant Creutzfeldt-Jakob Disease Diagnosed 7.5 Years after Occupational Exposure. N Engl J Med. 2020 Jul 2;383(1):83-85.
3. Brown P, Gibbs Jr CJ, Rodger-Johnson P, Asher DM, Sulima MP, Bacote A, Goldfard LG, Gajdusek DC. Human Spongiform Encephalopathy: The National Institutes of Health Series of 300 cases of experimentally transmitted disease. Ann Neurol 1994; 35: 513-529.
4. Wong BS, Green AJ, Li R, Xie Z, Pan T, Liu T, Chen SG, Gambetti P, Sy MS. Absence of protease-resistant prion protein in the cerebrospinal fluid of Creutzfeldt-Jakob disease. J Pathol 2001; 194: 9-14.
5. Head MW, Ritchie D, Smith N, McLoughlin V, Nailon W, Samarad S, Masson S, Bishop M, McCardle L, Ironside JW. Peripheral tissue involvement in sporadic, iatrogenic and variant Creutzfeldt-Jakob disease: an immunohistochemical, quantitative and biochemical study. Am J Pathol 2004; 164: 143-153.