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MarkVCID Postmortem Procedures Best Practice Guidelines

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MarkVCID Consortium

By the MarkVCID Postmortem Procedures & Analysis Subcommittee
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Based in substantial part on the Biospecimen Best Practice Guidelines for the Alzheimer's Disease Centers, v3.0. Reproduced with permission. 24 June 2014 National Institute on Aging. Created and published by the NIA Biospecimen Task Force (Co-chairs Tatiana Foroud, PhD and Thomas J. Montine, MD, PhD).

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BRAIN GUIDELINE

All laboratories should follow documented standardized protocols for tissue collection, processing, storage, retrieval, and dissemination as well as for histologic methods and any other tissue-based assays. The following presents guidelines for current best practices for a research brain bank focused on Alzheimer's disease (AD) and related neurodegenerative diseases.

I. Prior to autopsy

A. Usual practice for research brain banks is brain autopsy only; however, to the extent possible, full autopsy should be considered and requested.

B. 24/7 on call autopsy coordinator, autopsy technician(s), and tissue bank technician(s) is optimal so collection may occur as rapidly as possible after death.

C. Autopsies should include individuals with documentation of research quality clinical work up and a diagnosis of Alzheimer's dementia, MCI, related neurodegenerative diseases, or cognitively normal.

D. Detailed clinical information is essential to maximize the research usefulness of brain donations. Responsibility for obtaining this information is largely outside of brain banking operations; however, databasing this information may occur within the brain bank or some other component of the research group:

- Sex, cause of death, age at death, date of last clinical assessment, relevant family history, medication history, diagnosis(es) of brain diseases, other diagnoses, duration of illness(es), relevant neuroimaging or other laboratory findings, and agonal conditions, *e.g*., fever, O_2 saturation, etc.

E. Acknowledgment of local institutional requirements (for example, we continue to be prohibited from any fresh/frozen tissue storage if the deceased is COVID positive at the time of autopsy).

II. At time of autopsy

A. Autopsies must be performed according to local consenting and IRB protocols, as well as in compliance with all hospital, municipal, state, and federal laws and regulations.

B. The goals are to ensure the safety of all personnel, to make the correct neuropathologic diagnosis(es), and to obtain and process brain regions in a manner that maximizes their research utility.

a. Always use universal precautions when handing human tissue or body fluids.
b. If prion disease is a consideration, then follow protocols published by the National Prion Disease Pathology Surveillance Center. (http://www.cjdsurveillance.com/). This procedure may be reserved for cases of short-duration dementia or those clinically suspected of harboring prion disease; some centers may use this protocol for all dementia cases because of the possibility that any case may have unsuspected CJD.
c. Minimal tissue block dissection should follow current NIA-AA guidelines[1,2]. Paraffin-embedded tissue blocks should be archived indefinitely.
    1. Include anterior watershed white matter
    2. Include posterior watershed cortex and underlying white matter
d. Best practice is to obtain a portion of cerebellar hemisphere sufficient to fill a tissue cassette from every case and to store at -80^{o}C as quickly as possible for potential future DNA preparation.
e. Best practice is to establish protocols to dissect and freeze as quickly as possible selected brain regions for potential future biochemical analyses. A variety of methods can be used and the details depend on the desired use of the tissue. Examples are flash freezing a few grams of tissue in liquid nitrogen, with or without isopentane, or between blocks of dry ice. Freezing tissue slabs is not considered best practice because of difficulty in subsequent dissection.
f. Support of collaborative research is a best practice. Additional brain samples and additional methods for optimal stabilization for specific assays should follow documented protocols.

g. Post mortem cerebrospinal fluid (CSF) may be collected, usually from the ventricular system. If it is, then best practice is to freeze at -80^{o}C in appropriate containers based on expected use (see CSF section) and to thaw only once for use.

C. Standard metrics should be collected from each autopsy; at a minimum, this should include post mortem interval (PMI), the time measured in hours between death and stabilization of the tissue. Measures of tissue integrity also should be considered; however, none has achieved consensus status. These include tissue pH as well as a variety of measures of molecular degeneration. Measurement of brain pH is recommended—either by using a surface pH electrode or by measuring pH of either ventricular fluid or homogenized brain using a standard pH electrode.

III. After autopsy

A. Histologic and immunohistochemical staining of standard tissue blocks should follow current NIA-AA guidelines[1,2]. Histologic slides should be archived for at least 10 years or longer depending on research needs or regulations.

B. Fixed tissue as well as frozen tissue and CSF also should be retained for at least 10 years, or longer depending on research needs or regulations.

C. All biospecimens should be stored in appropriately labeled containers with unique identifiers and in a regulated environment with safeguards against physical damage, temperature changes, severe weather, and natural disasters.

D. It is best practice that all biospecimens are stored in a manner that meets universal precautions, IRB oversight, and employee health safety regulations; permits further neuropathologic evaluation if needed; and optimizes future potential research use.

E. Best practice is to maintain an accurate and appropriately safeguarded inventory of accrued biospecimens, distributed biospecimens, and available tissue and fluid resources.

F. Biospecimen resource inventory should be linked with a database(s) that contains outcomes of neuropathologic evaluation, clinical information, and results from other investigations, *e.g*., genetic information, in a manner that is IRB compliant and meets the need for subject confidentiality, security, and informed consent provisions (see Informatics Guideline).

G. In addition to scientific advisory committees for the research group, a brain bank should regularly convene a Biospecimen Use Committee.

References

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2. Hyman BT, Phelps, CH, Beach, TG, Bigio, EH, Cairns, NJ, Carrillo, MC, Dickson, DW, Duyckaerts, C, Frosch, MP, et al. National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. Alzheimer’s Dement. 2012; 8:1-13.PMC3266529