



Department of Epidemiology, School of Public Health and Community Medicine, University of Washington

4311 11th Avenue NE #300
Seattle, WA 98105
phone: (206) 543-8637; fax: (206) 616-5927
e-mail: naccmail@u.washington.edu
website: <https://www.alz.washington.edu>

NACC Neuropathology (NP) Diagnosis Coding Guidebook

*Detailed, annotated explanations of the form on an item-level basis,
with instructions, operational definitions, and references*

(Version 9.1, September 2008)

***NOTE: Version 9 is NOT the most current version of the NP form and
is not to be used for autopsies conducted on or after January 27, 2014.
For the current version of the form, please visit <http://www.alz.washington.edu>.***

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NACC Neuropathologic Diagnosis Coding Guidebook

The NACC Neuropathologic Diagnosis Coding Guidebook contains procedures to be followed when completing the NACC Neuropathology Data Form. This guidebook is authored by the members of the ADC Neuropathology Core Leaders' Steering Committee.

Typographical Conventions

Instructions will appear as a sans serif font against a shaded background...sample text

General Instructions

1. Please answer all items for all subjects.
2. Explanation of allowable codes:
 - “Not done” and “Not assessed” – these responses are equivalent and some questions use one version or the other.
 - “Missing/unknown” – this response indicates the data is not available because it has been lost or is no longer retrievable.

DEMOGRAPHICS

1. MDS/UDS Patient ID
2. Date form completed
month day year
3. Neuropath ID
4. Gender..... (*M or F*)
5. Age at death *years*
6. Date of death.....
month day year

Please provide identification and demographic neuropathology information in questions 1– 6.

7. Does the brain have any gross or microscopic pathology (including any Alzheimer type pathology such as senile plaques and neurofibrillary tangles)?

(*mark one box*)

- 1 Yes
 2 No

(Note: For either response, items 8A through 24 must also be answered.)

Answer “no” only if the brain is completely devoid of any histopathologic changes. If there are only minimal Alzheimer type changes, please indicate this in the following questions.

ALZHEIMER TYPE PATHOLOGY

Alzheimer’s Disease. For all brains in which there is any degree of Alzheimer type pathology (ranging from a few senile plaques and neurofibrillary tangles to advanced Alzheimer’s Disease), please indicate the nature of the pathology according to commonly used pathological criteria.

Follow the published guidelines for these entries. Answer “not done” for all criteria not used.

8A. NIA/Reagan Institute neuropathological criteria used:

(*mark one box*)

- 1 High likelihood of dementia being due to Alzheimer’s disease
 2 Intermediate likelihood of dementia being due to Alzheimer’s disease
 3 Low likelihood of dementia being due to Alzheimer’s disease
 4 Criteria not met
 5 Not done
 9 Missing/unknown

(Hyman BT, Trojanowski JQ. Editorial on Consensus recommendations for the postmortem diagnosis of Alzheimer’s Disease from the National Institute on Aging and Reagan Institute Working Group on Diagnostic Criteria for the Neuropathological Assessment of Alzheimer’s Disease. *J Neuropathol Exp Neurol* 1997;56:1095-1097.)

8B. CERAD neuropathological criteria used:

(mark one box)

- 1 Definite Alzheimer's disease
- 2 Probable Alzheimer's disease
- 3 Possible Alzheimer's disease
- 4 Criteria not met
- 5 Not done
- 9 Missing/unknown

(Mirra SM, Hart MN, Terry RD. Making the diagnosis of Alzheimer's disease. A primer for practicing pathologists. Arch Pathol Lab Med 1993;117:132-144.)

8C. ADRDA/Khachaturian neuropathological criteria used:

(mark one box)

- 1 Alzheimer's disease
- 2 Criteria not met
- 3 Not done
- 9 Missing/unknown

(Khachaturian S. Diagnosis of Alzheimer's disease. Arch Neurol 1985;42:1097-1105.)

8D. Other or unspecified neuropathological criteria used (e.g., Tierney, etc.):

(mark one box)

- 1 Alzheimer's disease, unspecified
- 2 Criteria not met
- 3 Not done
- 9 Missing/unknown

Neurofibrillary Pathology. For all brains in which topographic staging of neurofibrillary degeneration was done, please indicate the stage with a number from 1–7. If Braak staging was not done, use number 8.

Indicate the stage according to the scheme proposed by Braak and Braak. While the original methods employed Gallyas stains, other stains for neurofibrillary pathology (e.g., tau immunostains, other silver stains or thioflavin-S) may be used. The focus is on the distribution of neurofibrillary tangles. (Nagy Z, Yilmazer-Hanke DM, Braak H, et al. Assessment of the pathological stages of Alzheimer's disease in thin paraffin sections: a comparative study. *Dementia & Geriatric Cognitive Disorders* 1998;9:140-144; Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. *Acta Neuropathol* 1991;82:239-259.)

9. Braak & Braak Neurofibrillary Stage.

(mark one box)

- 1 Stage I
- 2 Stage II
- 3 Stage III
- 4 Stage IV
- 5 Stage V
- 6 Stage VI
- 7 Neurofibrillary degeneration not present
- 8 Not assessed
- 9 Missing/unknown

Stages I–II correspond to NFT limited to the transentorhinal/entorhinal region; Stages III–IV to limbic stages; and Stages V–VI to neocortical stages. Stage VI implies involvement of primary cortices. Answer “not assessed” if topographic staging has not been done.

Plaque Score. For the most severely affected cortical region, please indicate the plaque score. Please use the Consortium to Establish a Registry of Alzheimer’s Disease (CERAD) standards for sparse, moderate, and frequent.

10. Neuritic plaques (plaques with argyrophilic dystrophic neurites with or without dense amyloid cores).

(mark one box)

- 1 Frequent neuritic plaques
- 2 Moderate neuritic plaques
- 3 Sparse neuritic plaques
- 4 No neuritic plaques
- 5 Not assessed
- 9 Missing/unknown

Neuritic plaques are considered to be plaques with argyrophilic, thioflavin-S-positive or tau-positive dystrophic neurites with or without dense amyloid cores. Answer “not assessed” if neuritic plaques have not been specifically analyzed.

11. Diffuse plaques (plaques with non-compact amyloid and no apparent dystrophic neurites).

(mark one box)

- 1 Frequent diffuse plaques
- 2 Moderate diffuse plaques
- 3 Sparse diffuse plaques
- 4 No diffuse plaques
- 5 Not assessed
- 9 Missing/unknown

Diffuse plaques are considered to be plaques with non-compact amyloid and no apparent dystrophic neurites. Answer "not assessed" if diffuse plaques have not been specifically analyzed.

ISCHEMIC, HEMORRHAGIC AND VASCULAR PATHOLOGY

This section is meant to indicate the presence of vascular pathology, but not the absolute burden, volume, or severity of change. More detailed information about lesion distribution, burden, etc is presumed to be part of a research database. Questions about severity of vascular pathology are of necessity subjective, since current methods to easily and consistently assess severity of vascular disease have not been validated or widely implemented. Even if infarcts, focal sclerosis and hemorrhages are not present, and there is evidence of vascular pathology, be sure to answer questions 12I through 12K to record information about severity of atherosclerotic, arteriosclerotic, and amyloid vascular pathology.

12. Is ischemic, hemorrhagic or vascular pathology present?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

(Note: Items 12A through 12L must also be answered.)

Please include atherosclerosis, arteriosclerosis or amyloid angiopathy.

12A. Are one or more large artery cerebral infarcts present?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

This category refers to infarcts larger than 1 cm in diameter in the distribution of large and medium sized meningocerebral vessels rather than small parenchymal vessels. Infarcts meeting these criteria are included regardless of the histologic age and include acute lesions as well as chronic cystic lesions.

12B. Are one or more cortical microinfarcts (including “granular atrophy”) present?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

This category refers to infarcts that are detected microscopically and may not be grossly visible, or may appear to the naked eye as cortical granularity. Microinfarcts in non-cortical areas should not be included in this category. Infarcts meeting these criteria are included regardless of the histologic age and include acute lesions as well as chronic cystic lesions.

12C. Are one or more lacunes (small artery infarcts and/or hemorrhages) present?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

This category refers to cystic/old infarcts or hemorrhages 1-cm or less in diameter that are usually grossly identified and in the distribution of small parenchymal vessels, most often in basal ganglia, thalamus, pons, cerebellum and cerebral white matter.

12D. Are single or multiple hemorrhages present?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

This category refers to cerebral hemorrhages, regardless of size in any region of the brain.

12E. Is subcortical arteriosclerotic leukoencephalopathy present?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

This category refers to multifocal or diffuse white matter pathology attributable to arteriosclerotic small vessel disease and will be associated with axonal and myelin loss in the centrum ovale, often associated with brain infarcts. White matter rarefaction confined to the immediate periventricular region (so-called periventricular “capping”) should not be included. (Roman GC. Senile dementia of the Binswanger type, a vascular form of dementia in the elderly; JAMA 1987;258:1782-1788 and Caplan LR. Binswanger’s disease – revisited. Neurology 1995;45:626-633.)

12F. Is cortical laminar necrosis present?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

This category refers to selective cortical necrosis of middle and lower cortical lamina most often associated with cerebral hypoperfusion and concentrated in border zones between major cerebral arteries.

12G. Is medial temporal lobe sclerosis (including hippocampal sclerosis) present?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

This category refers to selective neuronal loss and gliosis ("sclerosis") of medial temporal lobe structures. In the hippocampus, this is often limited to CA1 and the subiculum with variable involvement of endplate and CA2. The amygdala and entorhinal cortex may also be affected. In some cases there is a clear history of cerebral hypoperfusion. In others there may be a history of epilepsy. Similar pathology can also be seen in the setting of neurodegenerative disorders (e.g., FTD).

12H. Is atherosclerotic vascular pathology (of the circle of Willis) present?

(mark one box)

- 1 None
- 2 Mild
- 3 Moderate
- 4 Severe
- 5 Not assessed
- 9 Missing/unknown

Use this item to indicate the severity of atherosclerotic (intimal and medial fibrofatty atheromatous plaques) disease in the large (named) arteries at the base of the brain (i.e., the circle of Willis). The assessment is qualitative and subjective and should indicate an estimate of overall severity rather than an individual vessel.

12I. Is arteriosclerosis (small parenchymal arteriolar disease) present?

(mark one box)

- 1 None
- 2 Mild
- 3 Moderate
- 4 Severe
- 5 Not assessed
- 9 Missing/unknown

Use this item to indicate the severity of arteriosclerosis (arteriolosclerosis) (hyalinosis of the media and adventitia) of small parenchymal and/or leptomenigeal vessels. The assessment is qualitative and subjective and should indicate an estimate of overall severity rather than an individual vessel.

12J. Is amyloid angiopathy present?

(mark one box)

- 1 None
- 2 Mild
- 3 Moderate
- 4 Severe
- 5 Not assessed
- 9 Missing/unknown

Use this item to indicate the severity of cerebral amyloid angiopathy as demonstrated with special stains for amyloid (e.g., Congo red, thioflavin-S, or A β immunostaining). The assessment is qualitative and subjective, and should indicate an estimate of overall severity rather than an individual vessel.

12K. Is another type of angiopathy (e.g., CADASIL or arteritis) present?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

Use this item to indicate the presence of other forms of arteriopathy not mentioned in the above categories.

12L. Is there other pathology related to ischemic or vascular disease not previously specified present?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

This category refers to ischemic or vascular disease not specifically mentioned in the above categories.

Lewy Body Pathology. For all brains in which Lewy bodies are detected, indicate the presence and distribution of Lewy-related pathology. This classification is independent of the clinical presentation, which may be variable and include Parkinsonism, dementia, psychosis, sleep disorders, etc.

13A. Pathology is consistent with criteria of Consortium on Dementia with Lewy Bodies for:

(select only one)

- 1 Lewy body pathology, brainstem predominant type
- 2 Lewy body pathology, intermediate or transitional (limbic) type
- 3 Lewy body pathology, diffuse (neocortical) type
- 4 Lewy body pathology, unspecified or not further assessed
- 5 No Lewy bodies
- 6 Not assessed
- 9 Missing/unknown

13B. Likelihood that DLB Clinical Syndrome due to DLB Pathology:

(select only one)

- 1 Low
- 2 Intermediate
- 3 High
- 6 N/A (not applicable)
- 9 Missing/unknown

Characterization of Lewy body pathology should use guidelines set forth by “Consortium on Dementia with Lewy bodies.” (McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): Report of the consortium on DLB international workshop. *Neurology* 1996;47:1113-1124 and McKeith IG, Dickson DW, Lowe J, et al. Diagnosis and Management of Dementia with Lewy Bodies: Third report of the DLB Consortium, *Neurology* 2005, 65:1863-1872.) According to the 2005 guidelines, the preferred method of assessment is with immunohistochemistry for alpha-synuclein. If Lewy body pathology was assessed with ubiquitin or H&E stains (not synuclein), please specify “4 – Lewy body pathology, unspecified” as your answer.

The diffuse (neocortical) type implies involvement of neocortical areas beyond the limbic lobe. The transitional (limbic) type implies cortical involvement limited to limbic lobe. Cases with Lewy bodies limited to the amygdala were not specifically addressed in the Consortium criteria, but should be included in the transitional (limbic) type for the sake of this database.

The 2005 published criteria recommend semi-quantitative evaluation of Lewy bodies, similar to that used for CERAD plaque grading (absent, mild, moderate, severe, and very severe). Pathologic characterization of Lewy body pathology is to be performed independent of Alzheimer-related pathology for the sake of this neuropathologic database. However, Alzheimer pathology as recorded in the previous section, “Alzheimer Type Pathology” (question 8A) is used to answer question 13B, the “likelihood that DLB clinical syndrome was due to DLB pathology”, by use of the following, adapted from the 2005 guidelines:

	Alzheimer type pathology		
	NIA-Reagan Low (Braak stage 0-II)	NIA-Reagan Intermediate (Braak stage III-IV)	NIA-Reagan High (Braak stage V-VI)
Lewy body type pathology			
Brainstem-predominant	Low	Low	Low
Limbic (transitional)	High	Intermediate	Low
Diffuse neocortical	High	High	Intermediate

Frontotemporal degenerations (FTD). Use this for non-Alzheimer degenerative disorders that commonly have the brunt of cortical changes in frontal and temporal lobes, but may involve other cortical and subcortical regions and have variable clinical presentations, including frontal lobe dementia, progressive aphasia, progressive apraxia, etc.

Use this category for non-Alzheimer degenerative disorders that commonly have the brunt of cortical changes in frontal and temporal lobes, but may involve other cortical and subcortical regions and have variable clinical presentations, including frontal lobe dementia, progressive aphasia, progressive apraxia, etc. (Trojanowski JQ, Dickson D: Update on the neuropathological diagnosis of frontotemporal dementias. J Neuropathol Exp Neurol 2001;60:1123-1126.)

14A. Pick's Disease:

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

For sake of uniformity and consistency, Pick's disease in this database is considered to be the classic form of the disease, the form referred to as type A Pick's disease in the classification of Constantinidis (Constantinidis J, Richard J, Tissot R. Pick's disease. Histological and clinical correlations. Eur Neurol 1974;11:208.) Such cases have sharply circumscribed frontotemporal atrophy with argyrophilic Pick bodies and ballooned neurons ("Pick cells"). If there are no Pick bodies, then an alternative diagnosis should be used.

14B. Corticobasal degeneration:

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

Corticobasal degeneration should refer to a condition in which there is circumscribed atrophy, often in a parasagittal distribution and microscopically characterized by extensive tau-positive or Gallyas-positive thread-like structures in gray and white matter of affected cortices, as well as the basal ganglia, thalamus and rostral brainstem. While ballooned neurons were emphasized in original description and are usually present, they are not essential to the diagnosis. Most cases will have tau-positive plaque-like structures, so-called astrocytic plaques.

14C. Progressive supranuclear palsy:

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

Progressive supranuclear palsy should refer to a condition with tau pathology in the basal ganglia, thalamus, brainstem and cerebellum. Original descriptions emphasized globose neurofibrillary tangles, but tau-positive or Gallyas-positive glial inclusions, both astrocytic (tufted astrocytes) and oligodendroglial (coiled bodies) are a constant finding. Thread-like structures are also common, especially in the diencephalon and brainstem. Cortical involvement is variable, but often relatively restricted to the peri-Rolandic region.

14D. Frontotemporal dementia and Parkinsonism with tau-positive or argyrophilic inclusions:

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

This classification will be used most often for cases of frontotemporal dementia and Parkinsonism linked to chromosome 17 (FTDP-17). Most cases have pathology that overlaps with CBD, PSP or Pick's disease and are associated with mutations in the Tau gene. Occasional cases with similar and extensive tau pathology in neurons and/or glia of the cortex and deep gray matter will have no family history or Tau mutations.

14E. Tauopathy, other (e.g., tangle-only dementia and argyrophilic grain dementia):

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

Use this for non-Alzheimer degenerative disorders that have tau-positive or Gallyas-positive neuronal and/or glial lesions, but do not fit into any of the above groups. Argyrophilic grain disease should be used for cases with tau-positive or Gallyas-positive grains restricted to limbic and peri-limbic regions as originally described by Braak et al. (Braak H, Braak E. Cortical and subcortical argyrophilic grains characterize a disease associated with adult onset dementia. *Neuropathol Appl Neurobiol* 1989;15:13-26) Most cases also have a few ballooned neurons in the limbic lobe. Tangle-only or tangle-predominant dementia should have the brunt of neurofibrillary degeneration in the medial temporal lobe, often with many extracellular neurofibrillary tangles (Jellinger KA, Brancher C. Senile dementia with tangles (tangle predominant form of senile dementia.) *Brain Pathol* 1998;8:367-376). Presence of non-neuritic, diffuse amyloid plaques does not exclude this diagnosis.

14F. FTD with ubiquitin-positive (tau-negative) inclusions:

(mark one box)

- 1 FTD with motor neuron disease
- 2 FTD without motor neuron disease
- 3 None present
- 4 Not assessed
- 9 Missing/unknown

Use this for non-Alzheimer degenerative disorders with focal atrophy of frontal, temporal or frontotemporal regions and relatively nonspecific histopathology with routine histopathologic methods, as well as with tau and synuclein immunostaining. Ubiquitin immunostaining will show perikaryal inclusions in affected cortices and often in the dentate fascia of the hippocampus. Many cases will show striatal or substantia nigra pathology and many have white matter changes, as well. Some cases will have clinical and/or pathologic evidence of motor neuron disease, but others will not. If immunohistochemical characterization has not been performed, list the case as FTD “not otherwise specified” (see question 14H).

14G. Is there FTD with no distinctive histopathology (tau-negative, ubiquitin-negative, and no argyrophilic inclusions)?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

Use this for non-Alzheimer degenerative disorders with focal atrophy of frontal, temporal or frontotemporal regions and relatively nonspecific histopathology with routine histopathologic methods, as well as with tau, synuclein and ubiquitin immunostaining. If immunohistochemical characterization has not been performed, list the case as FTD “not otherwise specified” (see question 14H).

14H. Was FTD “not otherwise specified” present (e.g., “immunostaining for ubiquitin and tau not done”)?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

Use this for non-Alzheimer degenerative disorders with nonspecific histopathology that do not clearly fit the above categories or in which immunohistochemical or biochemical characterization is not available or has not been done.

Prion-related disorders:

15A. Is Creutzfeldt-Jakob disease or variant CJD present?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

Respond "yes" if the case has definite CJD. Such cases would have confirmation with either immunohistochemistry or western blot. If the case has spongiform change, but has not been confirmed with immunohistochemistry or western blot, it should be listed under "Other Major Pathologic Disorders" as "CJD, unconfirmed" (see question 16B).

15B. Are other prion diseases present (e.g., Gerstmann-Straussler syndrome)?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

Respond "yes" if the case has definite prion disease, other than CJD or variant CJD. Such cases would have confirmation with either immunohistochemistry or western blot. If the case has spongiform change, but has not been confirmed with immunohistochemistry or western blot, it should be listed under "Other Major Pathologic Disorders" as "CJD, unconfirmed" (see question 16B).

Other major pathologic disorders (e.g., infectious, immunologic, metabolic, neoplastic, toxic or degenerative).

16A. Are other major pathologic disorders present (not addressed by questions 8–15)?

(mark one box)

- 1 Yes
- 2 No
- 3 Not assessed
- 9 Missing/unknown

SKIP: If 2, 3 or 9, go to #17A.

16B. If 16A is yes, specify below (one disorder per line):

- 1 _____
- 2 _____
- 3 _____

Use this section to record infectious, immunologic, metabolic, neoplastic, toxic or degenerative disease processes. If there are more than three disorders present, enter the three most descriptive in the space provided and omit the other disorders.

GENETICS & FAMILY HISTORY

17A. Family history information relevant to neuropathologic diagnosis. Choose one of the following categories that most accurately describes the **family** information available:

(mark one box)

- 1 Family history of similar neurodegenerative disorder
- 2 Family history of other (dissimilar) neurodegenerative disorder
- 3 No family history of similar or dissimilar neurodegenerative disorder
- 4 Family history of both similar and dissimilar neurodegenerative disorder
- 9 Family history unknown/not available/missing

SKIP: If 1, 3 or 9, go to #18A.

17B. If 17A is 2 or 4, specify disorder: _____

Choose one of the following categories that most accurately describes the family information available. If there is more than one relevant disorder in the family history, enter the most descriptive in the space provided and omit the other(s).

Genetic variants or polymorphisms. For each of the following three common genetic variants or polymorphisms, choose the patient's genotype, if known; select "not available or not assessed" if unknown:

18A. Apolipoprotein-E:

(mark one box)

- 1 e3, e3
- 2 e3, e4
- 3 e3, e2
- 4 e4, e4
- 5 e4, e2
- 6 e2, e2
- 9 Missing/unknown/not assessed

One of the major genetic risk factors for Alzheimer's disease is apolipoprotein-E. Please note the genotype, if known.

18B. Tau haplotype:

(mark one box)

- 1 H1, H1
- 2 H1, H2
- 3 H2, H2
- 4 Other polymorphism (e.g., A0)
- 9 Missing/unknown/not assessed

For tauopathies such as PSP and CBD, there is increased frequency of the H1 haplotype in the tau gene. It may also be increased in Parkinson's disease. Other polymorphisms in the tau gene have also been described, such as the A0 dinucleotide repeat. If known, please include. (Baker M, Litvan I, Houlden H, et al. Association of an extended haplotype in the tau gene with progressive supranuclear palsy. Hum Molec Genetics 1999;8:711-715.)

18C. PRNP codon 129:

(mark one box)

- 1 M, M
- 2 M, V
- 3 V, V
- 9 Missing/unknown/not assessed

For prion cases the polymorphism (methionine or valine) at codon 129 influences the phenotype.

19. Genetic or chromosomal abnormalities. Choose below the one known genetic or chromosomal abnormality that best describes the subject:

(mark one box)

- 1 APP mutation
- 2 PS1 mutation
- 3 PS2 mutation
- 4 Tau mutation
- 5 α -Synuclein mutation
- 6 Parkin mutation
- 7 PRNP mutation
- 8 Huntingtin mutation
- 9 Notch 3 mutation (CADASIL)
- 10 Other known genetic mutation (e.g., ABri, neuroserpin)
- 11 Down syndrome
- 12 Other chromosomal abnormality
- 13 No known genetic or chromosomal abnormality
- 50 Not assessed
- 99 Missing/unknown

Genetic information on the case is recorded here. Please choose "13" when a reasonable clinical evaluation has provided no indication that one of the specific known genetic or chromosomal abnormalities listed should be used to characterize this case. Please choose "50" when neither sufficient clinical work-up nor genetic testing to reasonably observe whether one of the conditions listed might be present has been performed.

20. What are the primary and contributing pathologic diagnoses or features which you judge to be responsible for the subject's cognitive status?

NOTE: *Mark only one diagnosis as "primary"; any number may be marked as "contributing".*

Specify only one diagnosis as "primary"; any number may be marked as "contributing" (check the appropriate box(es) for each additional diagnosis).

<u>Primary</u>	<u>Contributing</u>	
<input type="checkbox"/> A1	<input type="checkbox"/> A2	Normal brain (NC) Normal control.
<input type="checkbox"/> B1	<input type="checkbox"/> B2	AD pathology present but insufficient for AD diagnosis This diagnosis is used for NIA/Reagan low likelihood, or cases which are not classifiable by NIA/Reagan criteria. This category has been added for normal controls with low level AD pathology, such as cognitively normal individuals with Braak stage III or IV and moderate or frequent plaques, subjects with MCI, other cognitive deficits and early dementia)
<input type="checkbox"/> C1	<input type="checkbox"/> C2	Alzheimer disease (AD) Refer to questions 8, 9, and 10 for plaque load, CERAD grade, Braak stage, NIA/Reagan category.
<input type="checkbox"/> D1	<input type="checkbox"/> D2	Lewy body disease, with or without AD Refer to question 13 for details and staging.
<input type="checkbox"/> E1	<input type="checkbox"/> E2	Vascular disease Refer to question 12 for details, use in this diagnosis section if it is relevant to the dementia.
<input type="checkbox"/> F1	<input type="checkbox"/> F2	FTLD Refer to question 14 for sub-type.
<input type="checkbox"/> G1	<input type="checkbox"/> G2	Hippocampal sclerosis Can be related to either vascular disease or FTLD.
<input type="checkbox"/> H1	<input type="checkbox"/> H2	Prion-associated disease
<input type="checkbox"/> I1	<input type="checkbox"/> I2	Other (specify): _____
<input type="checkbox"/> J1	<input type="checkbox"/> J2	Other (specify): _____
<input type="checkbox"/> K1	<input type="checkbox"/> K2	Other (specify): _____ Any other neurologic or cognitive condition—Parkinson disease, ALS, MSA, SCA, etc.

Brain Tissue and Post Mortem CSF. Use this section to record information related to the storage and accessibility of brain tissue and post mortem CSF at your Center.

21. Is banked frozen brain tissue accessible?

(mark one box)

- 1 Yes
 2 No

22. Is formalin-fixed brain tissue accessible?

(mark one box)

- 1 Yes
 2 No

23. Are paraffin-embedded blocks of brain tissue accessible?

(mark one box)

- 1 Yes
 2 No

24. Is banked postmortem cerebrospinal fluid (CSF) accessible?

(mark one box)

- 1 Yes
 2 No

Check “yes” only if: (a) there is hard evidence that the specimen was taken; (b) there is some evidence that it was stored at your ADC; (c) there is a reasonable likelihood that the specimen, or any remaining portion, could be located at your ADC; and (d) the process of locating the specimen would be routine if ordinary effort were applied.

Check “no” if the indicated specimen is not stored in an easily accessible location at your Center.

REFERENCE CITATIONS

Page 2:

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Page 3:

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