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Neurology "Practice Parameters: Diagnosis and Evaluation of Dementia1" published in 1994 and updated in 2001 – but not since. As well as by the TriAD Advisory Board, 1996; the Canadian Consensus Conference on Dementia, 1999; and other literature regarding the work-up of dementia. Unfortunately, these prior criteria were last updated as of March 2009.

The original criteria for the clinical diagnosis of Alzheimer's disease (AD) were established in 1984. The National Institute on Aging (NIA) and the Alzheimer's Association sponsored a series of advisory round table meetings in 2009 whose purpose was to establish a process for revising diagnostic and research criteria for AD. The task was to formulating diagnostic criteria phases of the disease: the dementia phase; the symptomatic, pre-dementia phase; and the asymptomatic, preclinical phase of AD. Two notable differences from the AD criteria published in 1984 are incorporation of **biomarkers** of the underlying disease state and formalization of different stages of disease in the diagnostic criteria. There was a broad consensus that additional work is needed to validate the application of biomarkers for diagnostic purposes. In the revised NIA-Alzheimer's Association criteria, a semantic and conceptual distinction is made between AD pathophysiological processes and clinically observable syndromes that result, whereas this distinction was blurred in the 1984 criteria. The core clinical criteria of the recommendations regarding AD dementia and MCI due to AD are intended to guide diagnosis in the clinical setting. However, the recommendations of the **preclinical AD workgroup** are intended purely for research purposes.

Biomarkers (Aβ PET or CSF, tau CSF, FDG PET and structural MRI) are used in the revised definitions of AD in all three-disease phases, but the role of biomarkers differs somewhat in each of these stages. In the preclinical phase, biomarkers are used to establish the presence of AD-P in research subjects with no or very subtle overt symptoms. In both the MCI and AD dementia criteria, clinical diagnoses are paramount and biomarkers are complimentary. In the symptomatic predementia, MCI, phase biomarkers are used to establish the underlying etiology responsible for the clinical deficit. Biomarker severity, particularly neuronal injury biomarkers, also indicates the likelihood of imminent progression to AD dementia. In the dementia phase, biomarkers are used to increase or decrease, depending on the results, the level of certainty that AD-P underlies the dementia in an individual. The two major classes of biomarkers are treated equivalently in the MCI and dementia criteria. In contrast, they are ranked in a temporal hierarchy in the preclinical criteria, in that amyloid biomarkers become abnormal first and neuronal injury biomarkers become abnormal later. This temporal ordering notion is central to the staging proposed in the preclinical research criteria. The more conservative use for biomarkers in symptomatic subjects was felt to be a judicious approach pending more definitive outcomes research in this area.

In summary, the new criteria for AD are presented in three new documents, although the process is a continuous one with sometimes difficult-to-define boundaries between each discrete category. The evidence for preclinical AD is based almost entirely on AD biomarkers. Criteria for the earliest symptomatic manifestations, the MCI stage, represent a sharpening of previous efforts to define MCI. The MCI criteria also define an entity of MCI owing to AD-P, based on the conjunction of the clinical diagnosis and the presence of AD-P biomarkers. Finally, a revision of the 1984 criteria for dementia because of AD is provided. The criteria for probable AD dementia expand the breadth of the 1984 criteria and include biomarker enhancements to the diagnosis of AD dementia. Ultimately, it is hoped that the scientific knowledge gained over the past quarter of a century, leading to the reconceptualization of "Alzheimer's disease" proposed by the NIA-Alzheimer's Association workgroup, will result in improved diagnosis and ultimately in effective disease-modifying therapy.

ESSENTIAL CLINICAL components:

1) History
2) Physical exam
3) Neurologic exam
4) Mini-Mental status exam (MMSE) or Montreal Cognitive Assessment (MoCA)
5) Screening for depression
6) Laboratory analysis (including thyroid function tests, serum B12)
7) Neuroimaging with non-contrast MRI; or the use of contrast/non-contrast volumetric MRI imaging (volumetric pre-contrast sagittal T1 MPRAGE for Neuroreader Analysis and post contrast: sagittal MPRGE).

GUIDELINE

1) The DSM-5 definition of dementia is reliable and should be used. However, several notable changes occurred in the DSM-5 definition of "dementia" (now called Major Neurocognitive Disorder):

People previously diagnosed, as having "Mild Alzheimer's disease" (by DSM-IV criteria) would be classified as having Mild Cognitive Impairment (Minor Neurocognitive Disorder). MCI was recognized as an intermittent stage between "normal" loss of cognitive function that comes with age, and the development of Dementia. These terms had been associated with Alzheimer's disease whereas with DSM-5 the terms are non-specific and classify the degree of neurocognitive disorder rather than a specific disease subtype. Minor Neurocognitive Disorder is a decline in cognitive functioning due to loss in at least two cognitive domains (such as memory and language), but does not interfere with everyday activities. Major Neurocognitive Disorder Cognitive involves deficits across at least two cognitive domains which interfere with independence in everyday activities (e.g., at a minimum requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications).

2) The National Institute of Neurologic, Communicative Disorders and Stroke-AD and

The National Institute on Aging (NIA) and the Alzheimer's Association 2009 criteria has replaced related Disorders Association 1984 (NINCDS-ADRDA) criteria for AD. These groups sponsored a series of advisory round table meetings in 2009 whose purpose was to establish a process for revising diagnostic and research criteria for AD. The task was to formulating

diagnostic criteria phases of the disease: the dementia phase; the symptomatic, pre-dementia phase; and the asymptomatic, preclinical phase of AD.

3) Diagnostic criteria for vascular dementia, dementia with Lewy bodies, and Frontotemporal dementia should be used as referenced in DSM-5. Major and Mild Neurocognitive Disorder (NCD) may be due to any cause of dementia inclusive of Alzheimer's disease, Vascular disease, Traumatic Brain Injury, Lewy body disease amongst several others.

4) Structural neuroimaging with a non-contrast MR scan in the initial evaluation of patients with dementia is appropriate; however, the use of contrast/non-contrast volumetric MRI imaging is of utility in specific cases (volumetric pre-contrast sagittal T1 MPRAGE for Neuroreader Analysis and post contrast: sagittal MPRGE) a structural imaging can reveal tumors, evidence of small or large strokes, and damage from severe head trauma or a buildup of fluid in the brain (e.g. normal pressure hydrocephalus).

5) In cases where the diagnosis is uncertain regarding the differentiating between AD and frontotemporal dementia (FTD), dementia with Lewy bodies (DLB) or vascular dementia (VaD), imaging with fluorodeoxy-glucose positron emission tomography (FDG-PET) may be considered.

6) There are currently no genetic markers recommended for routine diagnostic purposes. Researchers have identified certain genes that increase the risk of developing Alzheimer's and other rare "deterministic" genes that directly cause Alzheimer's. Although genetic tests are available for some of these genes, there is no clear role for routine genetic testing for Alzheimer's disease in the clinician's diagnostic assessment.

7) Screening for depression, B12 deficiency, folate deficiency, and hypothyroidism should be routinely performed. In some cases one would also test for thiamine deficiency.

8) Screening for syphilis in patients with dementia is not justified unless clinical suspicion for neurosyphilis is present.

9) Neuropsychological evaluations are typically requested to assist healthcare providers in determining if functions of the brain, such as memory, attention, problem solving, etc., are functioning at expected levels. Doctors usually request a Neuropsychological evaluation when a patient reports difficulty with memory or thinking. Often family members may notice the changes before the patient is aware of problems. Medical, neurological, psychological or hereditary issues can cause changes in brain abilities.

Some of the conditions that can be successfully differentiated by neurocognitive testing include:

Alzheimer's disease
Frontotemporal dementias/other dementias
Parkinson's disease and other movement disorders, including deep brain stimulation (DBS)
Epilepsy/seizure disorders

Head injuries/sports concussion
Brain tumors
Brain infections (encephalitis, meningitis, etc.)
Sleep apnea and other sleep disorders
Depression
Strokes
Exposure to pesticides and other toxic chemicals
Cerebrovascular disease
Autoimmune disorders such as Multiple Sclerosis
Capacity/competency issues
Normal Pressure Hydrocephalus

Jump to Section Go

2. Criteria for all-cause dementia: Core clinical criteria

In this section, we outline core clinical criteria to be used in all clinical settings. Because there are many causes of dementia, we will first outline the criteria for all-cause dementia.

The diagnosis of dementia is intended to encompass the spectrum of severity, ranging from the mildest to the most severe stages of dementia. The methodology for staging of dementia severity was beyond the charge of the workgroup. Dementia is diagnosed when there are cognitive or behavioral (neuropsychiatric) symptoms that:

1. Interfere with the ability to function at work or at usual activities; and
2. Represent a decline from previous levels of functioning and performing; and
3. Are not explained by delirium or major psychiatric disorder;
4. Cognitive impairment is detected and diagnosed through a combination of (1) history-taking from the patient and a knowledgeable informant and (2) an objective cognitive assessment, either a "bedside" mental status examination or neuropsychological testing. Neuropsychological testing should be performed when the routine history and bedside mental status examination cannot provide a confident diagnosis.
5. The cognitive or behavioral impairment involves a minimum of two of the following domains:
    a. Impaired ability to acquire and remember new information—symptoms include: repetitive questions or conversations, misplacing personal belongings, forgetting events or appointments, getting lost on a familiar route.
    b. Impaired reasoning and handling of complex tasks, poor judgment—symptoms include: poor understanding of safety risks, inability to manage finances, poor decision-making ability, inability to plan complex or sequential activities.
    c. Impaired visuospatial abilities—symptoms include: inability to recognize faces or common objects or to find objects in direct view despite good acuity, inability to operate simple implements, or orient clothing to the body.
    d. Impaired language functions (speaking, reading, writing)—symptoms include: difficulty thinking of common words while speaking, hesitations; speech, spelling, and writing errors.
    e. Changes in personality, behavior, or comportment—symptoms include: uncharacteristic mood fluctuations such as agitation, impaired motivation, initiative, apathy, loss of drive, social withdrawal, decreased interest in previous activities, loss of empathy, compulsive or obsessive behaviors, socially unacceptable behaviors.

The differentiation of dementia from MCI (see companion article [5] on the diagnosis of MCI) rests on the determination of whether or not there is significant interference in the ability to function at work or in usual daily activities. This is inherently a clinical judgment made by a skilled clinician on the basis of the individual circumstances of the patient and the description of daily affairs of the patient obtained from the patient *and* from a knowledgeable informant.

Table 1

AD dementia criteria incorporating biomarkers

Diagnostic category	Biomarker probability of AD etiology	Aβ (PET or CSF)	Neuronal injury (CSF tau, FDG-PET, structural MRI)
Probable AD dementia			
Based on clinical criteria	Uninformative	Unavailable, conflicting, or indeterminate	Unavailable, conflicting, or indeterminate
With three levels of evidence of AD pathophysiological process	Intermediate	Unavailable or indeterminate	Positive
	Intermediate	Positive	Unavailable or indeterminate
	High	Positive	Positive
Possible AD dementia (atypical clinical presentation)			
Based on clinical criteria	Uninformative	Unavailable, conflicting, or indeterminate	Unavailable, conflicting, or indeterminate
With evidence of AD pathophysiological process	High but does not rule out second etiology	Positive	Positive
Dementia-unlikely due to AD	Lowest	Negative	Negative

Abbreviations: AD, Alzheimer's disease; Aβ, amyloid-beta; PET, positron emission tomography; CSF, cerebrospinal fluid; FDG, ^{18}fluorodeoxyglucose; MRI, magnetic resonance imaging.

Table 3

MCI criteria incorporating biomarkers

Diagnostic category	Biomarker probability of AD etiology	Aβ (PET or CSF)	Neuronal injury (tau, FDG, sMRI)
MCI–core clinical criteria	Uninformative	Conflicting/indeterminant/untested	Conflicting/indeterminant/untested
MCI due to AD—intermediate likelihood	Intermediate	Positive	Untested
		Untested	Positive
MCI due to AD—high likelihood	Highest	Positive	Positive
MCI—unlikely due to AD	Lowest	Negative	Negative

Abbreviations: AD, Alzheimer's disease; Aβ, amyloid beta peptide; PET, positron emission tomography; CSF, cerebrospinal fluid; FDG, fluorodeoxyglucose; sMRI, structural magnetic resonance imaging.

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