Biomarkers for Mild Cognitive Impairment (MCI) and Dementia: Practical Guide for Clinicians

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Purpose: Provide a quick, syndrome-based overview of commonly used tests that support dementia subtype diagnosis. Choose tests based on clinical phenotype, pretest probability, and how results will change management.

Condition / scenario	Preferred tests	Notes / interpretation
Vascular cognitive impairment / vascular dementia	Brain MRI (preferred), without contrast	Assess infarcts, lacunes, extensive white matter hyperintensities (WMH; often graded with Fazekas), cerebral microbleeds (lobar vs deep), enlarged perivascular spaces, and evidence of cerebral amyloid angiopathy.
Vascular cognitive impairment when MRI not feasible	Non-contrast head CT	Less sensitive for small vessel disease.
Alzheimer's disease (AD) biologic markers — blood	p-tau217; p-tau217/Aβ42 ratio; %p-tau217; A/T/N-style panel (A = Aβ42/40 ratio; T = p-tau181; N = neurofilament light [NfL]); p-tau181; APOE ε4; GFAP (glial fibrillary acidic protein)	p-tau217 (elevated in AD) is the preferred blood AD biomarker. %p-tau217 (p-tau217/total tau) may be preferred over p-tau217 alone in CKD stage 3b or higher. Aβ42/40 ratio may be low in AD but false positives have been reported (interpret cautiously). NfL reflects neurodegeneration and can be elevated with many brain-injury conditions. Consider APOE ε4 for ARIA risk counseling. GFAP is elevated in AD but also in other dementias and it may assist in diagnosis when there is diagnostic uncertainty
Alzheimer's disease (AD) biologic markers — CSF	Aβ42/40 ratio; p-tau181/Aβ42 ratio	Aβ42/40 is low in AD; p-tau181/Aβ42 is elevated.

Alzheimer's disease (AD) biologic markers — imaging	Amyloid PET	Use when blood and or CSF biomarkers are intermediate and there is clinical suspicion of AD.
Dementia with Lewy bodies (DLB) / Parkinsonian syndromes	FDG-PET; CSF α-synuclein seed amplification assay (SAA); skin biopsy (phosphorylated α-synuclein)	FDG-PET: lateral occipital hypometabolism is sensitive. "Cingulate island sign" (relative preservation of posterior cingulate) supports DLB and helps distinguish from AD (more specific).
Frontotemporal lobar degeneration (FTLD) / frontotemporal dementia	MRI without contrast; FDG-PET	MRI evaluates frontal/anterior temporal atrophy. FDG-PET shows a frontal/anterior temporal hypometabolism pattern that differs from the temporoparietal pattern typical of AD.
Limbic-predominant age-related TDP-43 encephalopathy (LATE)	MRI; FDG-PET	MRI: disproportionate amygdalar and hippocampal atrophy (Amygdalar Atrophy Scale: 0 = none, 1 = mild–moderate, 2 = severe), higher temporal-hippocampal volume ratio compared to AD. FDG-PET: temporo-limbic hypometabolism differs from the temporoparietal pattern seen in AD.

Guidelines for use

Principle	How to apply
Start with phenotype + reversible causes	History, collateral, medication review, mood/sleep, alcohol, cannabis, OSA, B12/TSH, and structural imaging.
Order biomarkers if initial evaluation indicates MCI / Dementia	Best done by dementia specialists and memory clinic / center teams
Multiple biomarker tests in atypical cases or mixed cases	Mixed dementia is common, especially in adults age 80 and older (as high as 2/3rds of cases). For example, p-tau217 plus FDG PET may be considered if AD and DLB suspected or AD and LATE suspected
Document pretest probability	Improves interpretation and helps explain false positives/negatives. Pretest probability is low in primary care clinics (thus, higher false positives) compared to Memory Centers / Clinics.

Prefer higher-quality reference labs for AD biomarkers	Consider Mayo Clinic Laboratories and Precivity Labs (Washington University) over LabCorp or Quest for blood and CSF tests.
Intermediate AD blood biomarker results	Consider CSF or amyloid PET, or re-test after 6 months.

Cautions: Biomarkers support (not replace) clinical diagnosis. Performance varies by assay and population; review your lab's validation, reference ranges, and known confounders (e.g., advanced age, vascular burden, inflammatory/rapidly progressive syndromes). Coordinate results disclosure with appropriate counseling.

Future biomarkers: MTBR-Tau243 plus %p-Tau217 may be better than just p-Tau217 and %p-Tau217.

References: Rabinovici et al. Updated Appropriate Use Criteria for Amyloid and Tau PET: A Report from the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging Workgroup. J Nuclear Med 2025. American College of Radiology ACR Appropriate Use Criteria 2024; JAMA Neurology Vascog 2, World Stroke Organization; Alzheimer's Association 2026 Facts and Figures; Roveta et al. Neurology 2026; Nelson et al. Annals of Neurology 2023. Alzheimer's Forum. 12/6/25.