



TESTING FOR AMYLOID BETA (A β) TO SUPPORT A DIAGNOSIS OF EARLY-STAGE ALZHEIMER'S DISEASE (AD)

Cerebrospinal fluid (CSF) test and positron emission tomography (PET) imaging

A β testing via CSF analysis or PET imaging can be used to confirm AD pathology^{1,2}

- A β -CSF testing and A β -PET imaging are highly concordant and highly diagnostically accurate³⁻⁵
- Evidence suggests that A β alterations in CSF may occur earlier than detectable by A β -PET imaging⁸
- As A β accumulates in the brain^{6,7}:
 - Concentrations of CSF A β_{42} decrease
 - Density of amyloid plaques visualized by PET increase

Brief Overview of A β Assessment Methods: CSF and PET^{4,9-12}

CSF		PET
Procedure done in an outpatient setting (either at a hospital, surgery center, or doctor's office)	Location	Performed at a diagnostic imaging center, either in a hospital, clinic, or office
Physician (neurologist or interventional radiologist), nurse practitioner, physician assistant	Clinician	Nuclear medicine specialist or radiologist
Example measures of biomarker levels in CSF: • A β_{42} • A $\beta_{42/40}$ ratio* • p-Tau/A β_{42} ratio [†]	Measure	Amyloid plaque density in the brain
Lumbar puncture is a routine procedure to collect CSF from a patient. The CSF is collected between the L3 and L4 or L4 and L5 vertebrae at a safe distance from the patient's spinal cord	Method	Brain imaging done with radioactive tracers to visualize the density of amyloid plaques
Low risk of side effects like headaches and back pain, which can be managed with atraumatic needles and local numbing	Most Common Side Effects	Noninvasive, but injection site reactions consisting of erythema, irritation, and pain are possible

*This ratio aims to compensate for interindividual variations in total A β production.

[†]Phosphorylated tau (p-Tau)/A β_{42} ratio provides improved concordance with amyloid PET when compared with a biomarker of A β alone.¹³

CONSIDERATIONS BEFORE REFERRING A PATIENT FOR A CSF TEST OR PET IMAGING FOR A β ASSESSMENT



Contraindications for CSF Testing¹²:

- Space-occupying lesions with mass effect, increase of intracranial pressure due to increased CSF pressure, or posterior fossa mass
- Anticoagulant medication, coagulopathy, or uncorrected bleeding diathesis
- Pre-existing skin infection at puncture site
- Complicated lumbosacral spine anatomy due to prior surgery, severe degenerative disease, or scoliosis



Contraindications for PET imaging^{14,15}:

- Obesity
- Claustrophobia



Regardless of testing method, best practices for A β testing include¹⁶:

- Establishing a clinical diagnosis of mild cognitive impairment (MCI) first
- Discussing ramifications of positive and negative results



For tips to discuss biomarker assessment and MCI due to AD with patients, use the [Patient Dialogue Guide: A \$\beta\$ Testing](#)

References: 1. Johnson KA, et al. *Alzheimers Dement*. 2013;9(1):e1-e16. 2. Shaw LM, et al. *Alzheimers Dement*. 2018;14(11):1505-1521. 3. Fagan AM, et al. *Ann Neurol*. 2006;59(3):512-519. 4. Lashley T, et al. *Dis Model Mech*. 2018;11(5):dmm031781. doi:10.1242/dmm.031781. 5. Zetterberg H, et al. *Exp Gerontol*. 2010;45(1):23-29. 6. Jack CR Jr, et al. *Alzheimers Dement*. 2018;14(4):535-562. 7. Wong DF, et al. *J Nucl Med*. 2010;51(6):913-920. 8. Palmqvist S, et al. *Brain*. 2016;139(pt 4):1226-1236. 9. Albert MS, et al. *Alzheimers Dement*. 2011;7(3):270-279. 10. Duits FH, et al. *Alzheimers Dement*. 2016;12(2):154-163. doi:10.1016/j.jalz.2015.08.003. 11. Suppiah S, et al. *Diagnostics (Basel)*. 2019;9(2):65. doi:10.3390/diagnostics9020065. 12. Engelborghs S, et al. *Alzheimers Dement (Amst)*. 2017;8:111-126. 13. Blennow K, et al. *Trends Pharmacol Sci*. 2015;36(5):297-309. 14. Ghanem MA, et al. *J Nucl Med Technol*. 2011;39(1):40-50. doi:10.2967/jnmt.110.078881. 15. MedlinePlus; U.S. National Library of Medicine. Brain PET Scan. Medical Encyclopedia Article. https://medlineplus.gov/ency/article/007341.htm?utm_source=email&utm_medium=share&utm_campaign=mplus_share. 16. Harkins K, et al. *Alzheimers Res Ther*. 2015;7(1):26. doi:10.1186/s13195-015-0112-7.