

Overview

Useful For

Assisting in the evaluation of patients in various research studies
This test is **not intended as** a screening or stand-alone diagnostic assay.

Highlights

This test measures the beta-amyloid peptides 1-40 and 1-42 and calculates the beta-amyloid ratio (1-42/1-40) in cerebrospinal fluid. The beta-amyloid ratio (1-42/1-40) is a surrogate marker of amyloid plaque burden, caused by increased deposition of beta-amyloid 1-42 in the brain.

Method Name

Chemiluminescent Immunoassay/Calculation

NY State Available

No

Reporting Name

Beta-Amyloid Panel, BioPharma, CSF

Aliases

Ab42/Ab40 ratio
Amyloid Beta 40
Amyloid Beta 42
Amyloid ratio
Beta-Amyloid 40
Beta-Amyloid 42

Specimen

Specimen Type

CSF

Specimen Required

Container/Tube:

Preferred: Sarstedt 1.5 mL tube (Ref. 72.703.600), Collect at least 750 mcL of cerebrospinal spinal fluid (CSF) or (≥50% full).

Acceptable: Sarstedt 10 mL tube Ref. 62.610.018, Collect at least 5 mL of CSF (≥50% full). All tubes should be filled to between 50% to 100% of the total empty container volume. Specimens received with less than the required fill volume may be rejected.

Specimen Volume: 0.75 to 1.5 mL or at least 50% container volume

Collection Instructions:

1. Perform lumbar puncture and discard the first 1 to 2 mL of CSF. Note: CSF collection should be performed by the gravity drip method.
2. Discard any visibly blood contaminated CSF.
3. Collect CSF directly into one of the listed collection tubes until the tube is at least 50% full.
4. If transporting frozen, freeze sample upright prior to placing in transport container.
5. If transporting refrigerate, tubes should be transported upright.

Note: Polystyrene collection tubes are not acceptable. Exposure of CSF to polystyrene tubes may result in falsely low beta-amyloid concentrations. For more information see Cautions.

Specimen Minimum Volume

0.75 mL

Reject Due To

Gross hemolysis	Reject
Thawing	Cold, ok; Warm >48 hours, Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Frozen (preferred)	90 days	
	Refrigerated	14 days	
	Ambient	48 hours	

Clinical & Interpretive
Clinical Information

One of the neuropathologic features found in the brain of patients with Alzheimer disease (AD) is the presence of plaques composed of beta-amyloid. The two beta-amyloid peptides evaluated by this assay are 1-40 and 1-42. Beta-amyloid 1-40 typically exists at a higher physiological concentration than beta-amyloid 1-42. In AD, beta-amyloid 1-42 accumulation, either by overproduction or decreased clearance, leads to aggregation into plaques and neurotoxicity. Beta-amyloid 1-40 is much less prone to aggregation, with levels remaining unchanged when comparing patients with AD to healthy individuals.

In cerebrospinal fluid (CSF), approximately a 50% reduction in beta-amyloid 1-42 concentrations has been observed in AD patients compared to the concentrations found in cognitively normal individuals. This is believed to be as consequence of the decrease in soluble beta-amyloid 1-42 in the brain interstitial fluid as the peptide becomes increasingly insoluble and form deposits in the form of large numbers of diffuse and neuritic plaques. Unlike beta-amyloid 1-42, the values for beta-amyloid 1-40 in CSF remain relatively stable in individuals regardless of the presence of amyloid-pathology.

Various studies have demonstrated that the use of the beta-amyloid ratio (1-42/1-40) increases diagnostic accuracy for AD versus use of beta-amyloid 1-42 alone. The beta-amyloid ratio (1-42/1-40) demonstrates high concordance with amyloid positron emission tomography (PET) when distinguishing amyloid deposition due to AD from alternative causes of mild cognitive impairment or dementia. In addition, the use of the CSF beta-amyloid ratio (1-42/1-40) could partially mitigate the effect of some preanalytical confounders that have been described to alter the results of beta-amyloid 1-42 in CSF.

Reference Values

 Beta-Amyloid Ratio (1-42/1-40): ≥ 0.073
Interpretation

A normal beta-amyloid ratio (1-42/1-40) of 0.073 and above is consistent with a negative (normal) amyloid positron emission tomography (PET) scan result. This result indicates a reduced likelihood that a patient's cognitive impairment is due to Alzheimer disease (AD).

A beta-amyloid ratio (1-42/1-40) between 0.059 and 0.072 (likely positive) is more likely consistent with a positive amyloid PET scan result. A likely positive result does not establish a diagnosis of AD or other cognitive disorder and has increased uncertainty in regard to amyloid PET positivity.

An abnormal beta-amyloid ratio (1-42/1-40) of 0.058 and below is consistent with a positive (abnormal) amyloid PET scan result. This result does not establish a diagnosis of AD or other cognitive disorder.

The performance of the beta-amyloid ratio (1-42/1-40) compared to amyloid PET is shown below and described as amyloid PET-positive predictive value (indicated as Predictive Value: PV):

Table.

Beta-amyloid ratio (1-42/1-40)	Amyloid PET			Amyloid PET-positive PV, %	95% CI, %
	Positive (n=199)	Negative (n=93)	Total (n=293)		
Positive (abnormal) (ratio \leq 0.058)	171	6	177	96.6	92.8-98.4
Likely positive (ratio 0.059 to 0.072)	13	9	22	59.1	38.7-66.7
Negative (ratio \geq 0.073)	15	78	93	16.1	10.0-24.9

Cautions

The beta-amyloid ratio (1-42/1-40) results must be interpreted in conjunction with other diagnostic tools such as neurological examination, neurobehavioral tests, imaging, and routine laboratory tests.

The safety and effectiveness of this test have not been established for monitoring the effect of any therapeutic product or for predicting development of dementia or other neurologic conditions.

The amyloid ratio (1-42/1-40) has not been shown to correlate with disease severity.

Results obtained with different assay methods or kits may be different and cannot be used interchangeably.

In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human anti-mouse antibodies or heterophile antibodies) which may cause interference in some immunoassays. Caution should be used in interpretation of results and the laboratory should be alerted if the result does not correlate with the clinical presentation.

Clinical Reference

1. Wiltfang J, Esselmann H, Bibl M, et al. Amyloid beta peptide ratio 42/40 but not A beta 42 correlates with phospho-Tau in patients with low- and high-CSF A beta 40 load. *J Neurochem.* 2007;101(4):1053-1059. doi: 10.1111/j.1471-4159.2006.04404.x
2. Dumurgier J, Schraen S, Gabelle A, et al. Cerebrospinal fluid amyloid-beta 42/40 ratio in clinical setting of memory centers: a multicentric study. *Alzheimers Res Ther.* 2015 ;7(1):30. doi:10.1186/s13195-015-0114-5
3. Gervaise-Henry C, Watfa G, Albuissou E, et al. Cerebrospinal fluid ABeta42/ABeta40 as a means to limiting tube- and storage-dependent pre-analytical variability in clinical setting. *J Alzheimers Dis.* 2017;57(2): 437-445. doi:10.3233/JAD-160865
4. Toombs J, Foiani MS, Wellington H, et al. Amyloid Beta peptides are differentially vulnerable to preanalytical surface exposure, an effect incompletely mitigated by the use of ratios. *Alzheimers Dement (Amst).* 2018;10:311-321. doi:10.1016/j.dadm.2018.02.005
5. Delaby C, Munoz L, Torres S, et al. Impact of CSF storage volume on the analysis of Alzheimer's disease biomarkers on an automated platform. *Clin Chim Acta.* 2019;490:98-101. doi:10.1016/j.cca.2018.12.021

Performance

Method Description

beta-Amyloid 1-40:

The Lumipulse G beta-Amyloid 1-40 is an assay system for the quantitative measurement of beta-amyloid 1-40 in cerebrospinal fluid (CSF) specimens based on chemiluminescent enzyme immunoassay (CLEIA) technology by a specific two-step sandwich immunoassay method on the Lumipulse G System. The specimen is added to the particle solution. The beta-amyloid 1-40 in the specimen specifically binds to anti-beta-amyloid 1-40 monoclonal mouse antibody on the particles and antigen-antibody immunocomplexes are formed. The particles are then washed and rinsed to remove unbound materials. Alkaline phosphatase labeled anti-beta-amyloid monoclonal antibody is added that specifically binds to the prior formed immunocomplexes on the particles and additional immunocomplexes are formed. The particles are washed and rinsed to remove unbound materials. Substrate solution is added and mixed with the particles.

3-(2'-spiroadamantane)-4-methoxy-4-(3''-phosphoryloxy) phenyl-1, 2 dioxetane disodium salt (AMPPD) contained in the substrate solution is dephosphorylated by the catalysis of alkaline phosphatase indirectly conjugated to particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD. The luminescent signal reflects the amount of beta-amyloid 1-40 in the sample. (Package insert: Lumipulse G B-Amyloid 1-40. Fujirebio Inc; 05/2022)

beta-Amyloid 1-42:

The Lumipulse G beta-amyloid 1-42 is an assay system for the quantitative measurement of beta-amyloid 1-42 in CSF specimens based on CLEIA technology by a specific two-step sandwich immunoassay method on the Lumipulse G System. The specimen and biotinylated antibody solution are both added to the antibody coated particle solution. The beta-amyloid 1-42 in the specimen specifically binds to anti-beta-amyloid 1-42 monoclonal mouse antibody on the particles and biotinylated mouse antibody. Biotinylated antibody-antigen immuno-complexes are formed. The particles are washed and rinsed to remove unbound materials. Alkaline phosphatase labeled streptavidin specifically binds to biotinylated immuno-complexes on the particles. The particles are washed and rinsed to remove unbound materials. Substrate solution is added and mixed with the particles. AMPPD contained in the substrate solution is dephosphorylated by the catalysis of alkaline phosphatase indirectly conjugated to particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD. The luminescent signal reflects the amount of beta-amyloid 1-42 present in the sample. (Package insert: Lumipulse G B-Amyloid 1-42. Fujirebio Inc; 05/2022)

Ratio:

The beta-amyloid ratio is calculated by using individual measurements of beta-amyloid 1-42 and beta-amyloid 1-40.

Day(s) Performed

Thursday

Report Available

1 to 7 days

Specimen Retention Time

12 months

Performing Laboratory Location

Rochester

CLIA Laboratory Number

24D1040592

Test Classification

For research use only. This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.