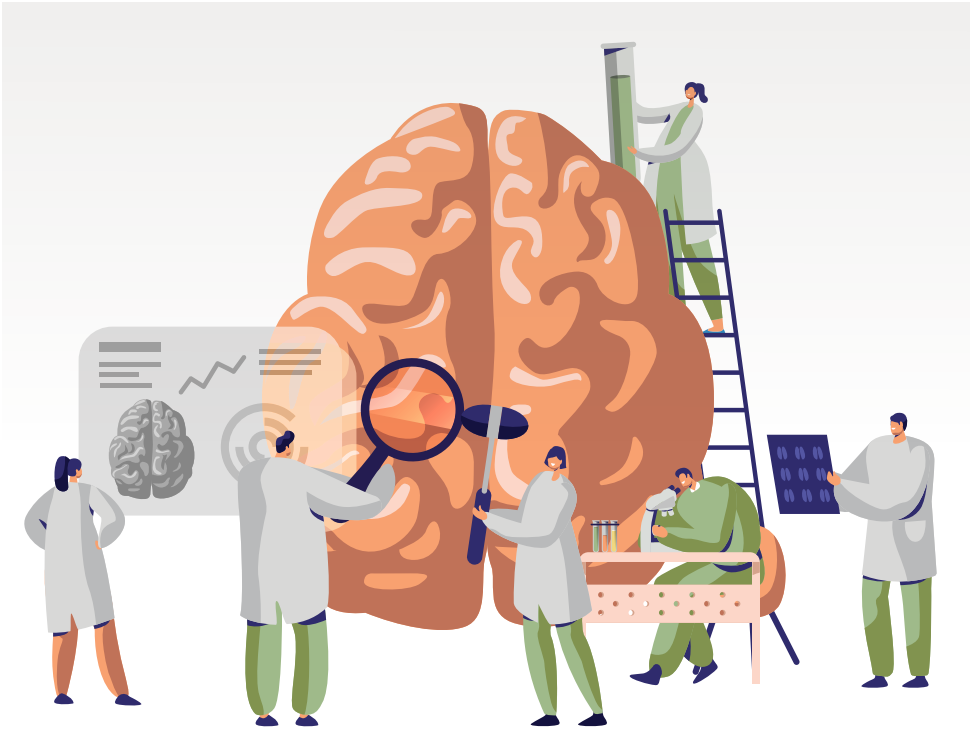
EUROIMMUN Medizinische Labordiagnostika AG

Preanalytics in dementia diagnostics

Recognising external impact factors and optimising procedures



- **Various external factors can strongly impact the results of dementia marker analyses**
- **Recommendations for clinical routine: standardised procedures from lumbar puncture to CSF analysis**

FOREWORD

> CSF analysis is now at the core of the diagnostic criteria for the diagnosis of Alzheimer's disease.
>
> Engelborghs et al., 2017.

> Currently the biomarkers $A\beta_{1-42}$, total tau and pTau(181) […] are clinically validated and established and can be used above all for positive diagnostics.
>
> S1 guideline "Lumbar puncture and CSF diagostics", 2019

The analysis of biomarkers in CSF has in recent years become an important component of Alzheimer's disease diagnostics. In particular, beta-amyloids in CSF are considered excellent biomarkers for amyloid pathology, and their relevance is emphasised in diagnostic guidelines.

Beta-amyloids are, however, subject to preanalytical influences to such an extent that using established CSF analysis procedures to perform Alzheimer's diagnostics can potentially lead to incorrect diagnoses. In order to counter this risk, it is essential to fundamentally understand the various impact factors in preanalytics. This is important for the laboratory staff directly involved as well as for clinicians, since the careful peformance of each step between lumbar puncture and CSF analysis contributes to the quality of the biomarker result.

In the last two decades intensive research has resulted in considerable advances in the understanding of preanalytical impact factors, and the number of published research papers is growing rapidly.

This brochure serves as a compendium for clinicians and laboratory doctors, providing an overview of the current status of preanalytics in Alzheimer's diagnostics. It also includes further information such as diagnostic guidelines, practical working steps in the laboratory and multiparameter interpretation of results. The most important pitfalls in CSF-based dementia diagnostics are explained in detail. Using concrete examples from representative studies, the effects of different laboratory practices on the measured beta-amyloid concentrations are demonstrated.

CONTENT

Diagnostic guidelines

S3 guideline "Dementia", 2016[1]

Published by the DGPPN and the DGN (Germany): detailed S3 guideline (currently being revised) including recommendations for CSF-based neurochemical dementia diagnostics

IWG recommendations for clinical diagnosis of Alzheimer's disease, 2021[2]

Published by the IWG: recommendations for diagnosing Alzheimer's disease in the diagnostic routine based on clinical and biomarker profiles.

NIA-AA recommendations for diagnostic guidelines for Alzheimer's disease, 2011[3]

Published by the NIA and the AA (USA): current criteria for dementia in the diagnostic routine with the main focus on clinical factors

S1 guideline "Lumbar puncture and CSF diagnostics", 2019[4]

Published by the DGN and the DGLN: detailed recommendations for diagnostic lumbar puncture, basic CSF diagnostics and their usage in differential diagnostics of e.g. dementia

Which parameters are relevant?

Recommended for routine:

Cell count, differential cell picture, glucose, lactate, oligoclonal bands, Reiber diagram (albumin ratio, IgG, IgA, IgM)

In suspected Alzheimer's disease:

$A\beta_{1\text{-}42}$, $A\beta_{1\text{-}40}$, total tau, pTau(181)

AA: Alzheimer's Association; **DGLN:** German Society for CSF Diagnostics and Clinical Neurochemistry e. V.; **DGN:** German Neurological Society e. V.; **DGPPN:** German Association for Psychiatry, Psychotherapy and Psychosomatics e. V.; **IWG:** International Working Group; **NIA:** National Institute on Aging

1. DGPPN and DGN. AWMF Register No. 038-013 (2016). https://www.awmf.org/leitlinien/detail/ll/038-013.html
2. Dubois B, et al. Lancet Neurol S1474-4422(21)00066-1 (2021). https://doi.org/10.1016/S1474-4422(21)00066-1
3. McKhann GM, et al. Alzheimers Dement 7(3): 263–269 (2011). https://doi.org/10.1016/j.jalz.2011.03.005
4. Abridged, translated version: Tumani H, et al. Neurol Res Pract 2(1):8 (2020). https://doi.org/10.1186/s42466-020-0051-z

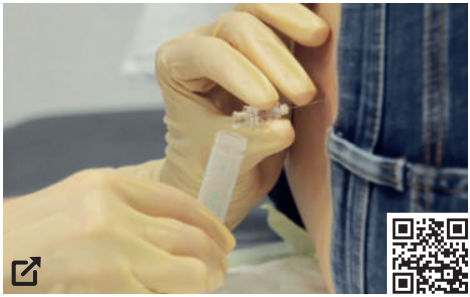
Lumbar puncture

Consensus guideline for lumbar puncture, 2017 [5]

Recommendations for performing lumbar puncture on patients with neurological diseases with the goal of minimising the risk of complications and reducing reservations about the procedure

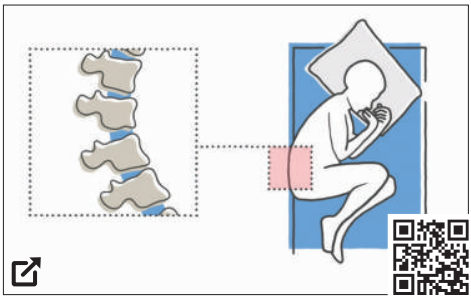
Didactic video on lumbar puncture for clinicians (5:08 min)

Published by VUmc Amsterdam: routine lumbar puncture – for training purposes, as an update on the state of the art, and to standardise the procedure for implementing CSF biomarkers in clinical practice; plus accompanying article [6]



Explanatory video on lumbar puncture for patients and nursing staff (3:45 min)

Published by VUmc Amsterdam: informs patients on the lumbar puncture procedure supplementarily to their medical consultation, helping them to understand the procedure, prepare for it and overcome any anxiety; plus accompanying article [7]



VUmc: VU University Medical Center

5. Engelborghs S, et al. Alzheimers Dement (Amst) 8:111-126 (2017). https://doi.org/10.1016/j.dadm.2017.04.007
6. Babapour Mofrad R, et al. Alzheimers Dement (Amst) 8:108–110 (2017). https://doi.org/10.1016/j.dadm.2017.04.008
7. Babapour Mofrad R, et al. Alzheimers Dement (Amst) 11:435-438 (2019). https://doi.org/10.1016/j.dadm.2019.04.005

Preanalytical impact factors

Sample collection	Transport	Laboratory
■ Collection method	■ Shaking	■ Tube transfer
■ Collection tube material	■ Temperature	■ Sample tube material
■ Tube size/ sample volume		■ Tube size/ sample volume
■ Blood contamination		■ Temperature
		■ Freezing/thawing
		■ Pipette tips

Typical preanalytical impact factors in CSF analysis for Alzheimer's diagnostics

Beta-amyloids are especially affected by preanalytical factors

Of the relevant analytes in Alzheimer's diagnostics, beta-amyloids (Aβ) are especially affected by preanalytical factors. There are many impact factors that, especially when they accumulate, can have a considerable negative effect on the measured concentration of analytes in CSF, resulting in false positive results. For example, the choice of consumables can strongly influence the analysis result. This should be taken into consideration in all aspects of sample handling, including sample collection, transport and laboratory work.

Since the isoforms $A\beta_{1-42}$ and $A\beta_{1-40}$ are subject to preanalytical impact factors to a similar extent, the relationship of the analytes to each other remains stable. Determination of the ratio of $A\beta_{1-42}$ and $A\beta_{1-40}$ yields more reliable results than with $A\beta_{1-42}$ alone. It should always be favoured over a single measurement.

See also ▶ Results (p. 21)

On the following pages relevant information from selected publications and current recommendations for preanalytics are presented.

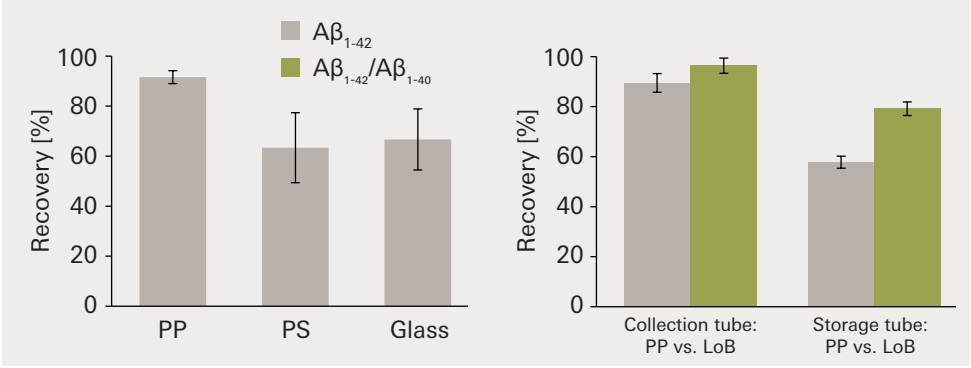
Sample collection

Impact of the tube

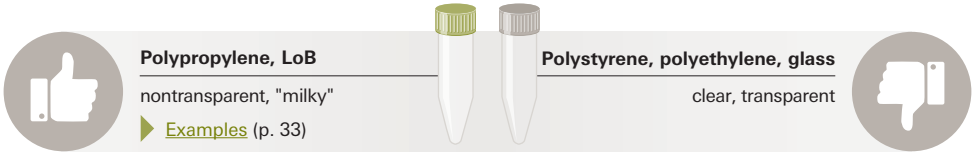
Material of choice: LoB or polypropylene

Studies have shown that beta-amyloids can irreversibly adsorb onto surfaces.[8,9] For reliable results the CSF should only come into contact with surfaces made of polypropylene (PP) or protein low-bind material (LoB). The latter is considered the gold standard in Aβ analytics, since the adsorption is hereby reduced to a minimum. Polystyrene (PS), polyethylene (PE) or glass must be avoided under all circumstances, since their usage can lead to false positive results – with corresponding diagnostic consequences.

► Determining the $Aβ_{1-42}$ to $Aβ_{1-40}$ ratio and using suitable materials yields more stable results.[9]



Impact of the tube material on the measured beta-amyloid concentration (modified from Andreasen et al., 1999 and Vanderstichele et al., 2016)



8. Andreasen N, at al. Arch Neurol 56(6):673-80 (1999). https://doi.org/10.1001/archneur.56.6.673
9. Vanderstichele H, et al. J Alzheimers Dis 53(3):1121-32 (2016). https://doi.org/10.3233/JAD-160286

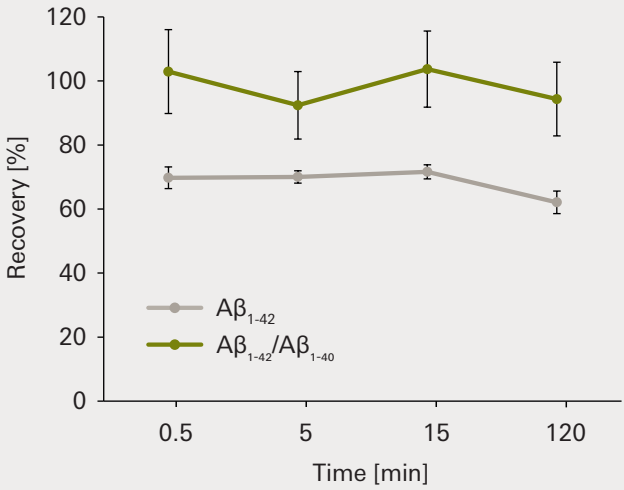
Sample collection

Adsorption kinetics

Adsorption already after 30 seconds

Beta-amyloid is adsorbed shortly after contact with surfaces of different materials and is then no longer determined in the analysis. The measured concentration of the analyte thus does not correspond to the original amount in the CSF sample. In a study it was shown that the adsorption occurs within 30 seconds and that the vessel walls are already saturated after this short time.[10]

► The $A\beta_{1-42}/A\beta_{1-40}$ ratio remains largely stable.



Measurable beta-amyloid quantity depending on the duration of contact with the sample tube (modified from Willemse et al., 2017)

10. Willemse E, et al. Alzheimers Dement 13(8):885-892 (2017). http://doi.org/10.1016/j.jalz.2017.01.010

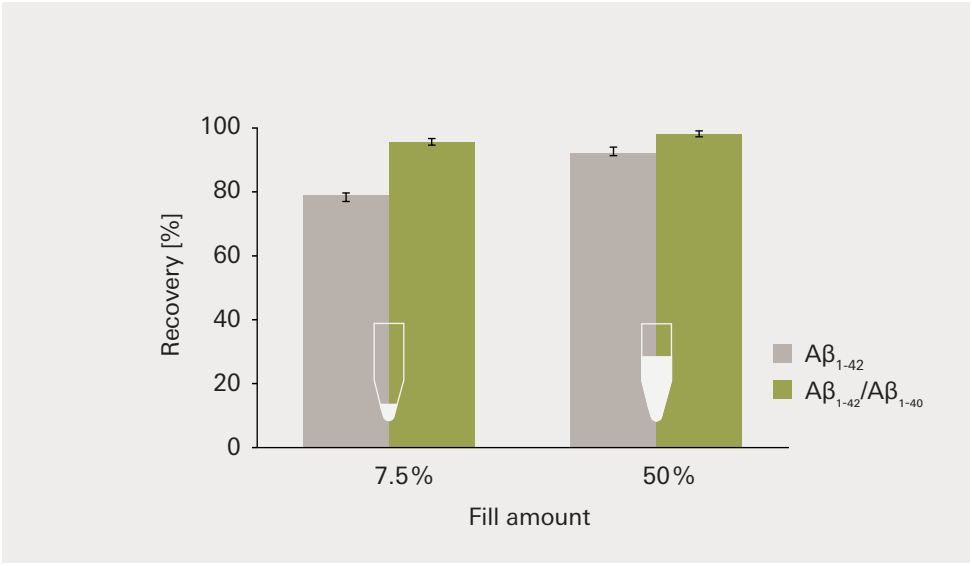
Sample collection

Correct volume

Low sample volumes lead to increased adsorption

The sample volume can also affect the measurable beta-amyloid quantity. The ratio of the sample volume to the surface area with which the sample comes into contact is decisive. In a study, a high ratio of contact surface to volume (150 µl vs. 1000 µl) led to more adsorption of $A\beta_{1-42}$. The tested volumes corresponded to a tube fill amount of 7.5 % or 50 %. [10]

► The $A\beta_{1-42}/A\beta_{1-40}$ ratio remains constant even with low volumes.



Measurable beta-amyloid quantity depending on the sample volume (modified from Willemse et al., 2017)

10. Willemse E, et al. Alzheimers Dement 13(8):885-892 (2017). http://doi.org/10.1016/j.jalz.2017.01.010

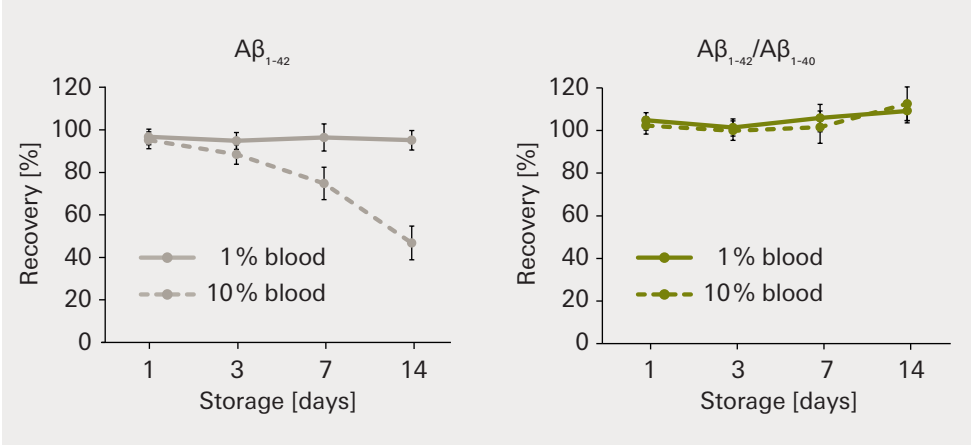
Sample collection

Blood contamination

Blood in the sample reduces the measurable beta-amyloid concentration

Blood contamination of the CSF can occur through mechanical trauma during the lumbar puncture. Depending on the amount of blood and the sample storage temperature and duration, strong effects on the measurable beta-amyloid concentration can be demonstrated. Study data show that an increasing degree of blood contamination leads to a reduced $A\beta_{1\text{-}42}$ value. This effect is measurable after just a few days even with optimal sample storage. [11]

► The extent of the loss of $A\beta_{1\text{-}42}$ and $A\beta_{1\text{-}40}$ in CSF is comparable. Thus, even with high levels of blood contamination the $A\beta_{1\text{-}42}/A\beta_{1\text{-}40}$ ratio is not affected and enables a stable measurement. With appropriate storage (+4 °C or -20 °C), additional centrifugation of the samples could prevent the negative effect of the blood on the measurable analyte quantity.



Impact of blood contamination on the measurable beta-amyloid quantity in CSF; storage at +4 °C (modified from Janelidze et al., 2019)

11. Janelidze S, et al. Alzheimers Res Ther 11(1):63 (2019). https://doi.org/10.1186/s13195-019-0517-9

Sample collection

Recommendations at a glance

The right way: from the puncture needle to sample storage

In order to avoid adsorption of beta-amyloids through unnecessary contact with consumables such as syringes, the CSF should be collected by the gravity drip method directly into the tubes from which it will be later taken for the analysis. Moreover, the use of an atraumatic puncture needle with a small diameter (22G) and the discarding of the first 2 ml of CSF reduce the risk of blood contamination. The tubes – exclusively LoB or PP – should be filled to at least 50 %.

If the analysis is not to be performed immediately on-site, it is recommended to freeze the CSF samples. In this way the impact of different factors (e.g. shaking or too high a temperature) can be prevented. Through this standardisation, samples sent by different clinicans are comparable. Furthermore, the cut-offs from many manufacturers of laboratory diagnostic tests are established using one-time frozen samples.

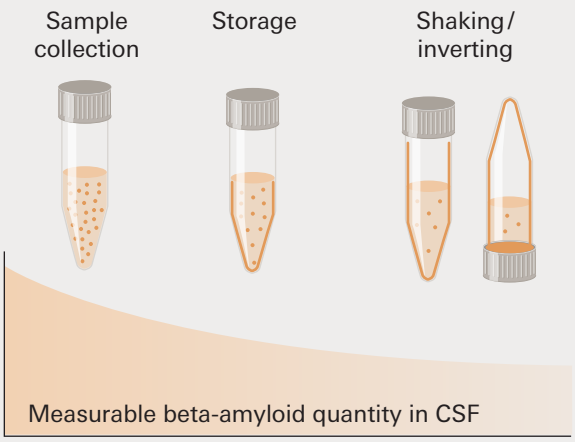
Puncture needle	Withdrawal method	Sample tube material
Atraumatic, small diameter (22G)	Using drip method directly into tube	LoB or polypropylene
CSF fraction	**Sample volume**	**After sample collection**
Do not use the first 2 ml for the biomarker analysis	Fill sample tubes to at least 50 %	No aliquotting, freeze immediately (-20 °C)

Transport

Correct storage

Avoid unnecessary material contact

A study showed that, for example, inversion and horizontal storage of CSF samples leads to a reduction in the measurable $A\beta_{1-42}$ quantity.[12] In addition, shaking movements during transport play a role. These effects can be countered by storage and transport of the samples in a frozen state. This is also an issue when using screw-cap tubes made of suitable LoB material, as some manufacturers supply these with lids made of unsuitable material (e.g. PE).



Schematic representation of the reduction in the measurable beta-amyloid quantity through adsorption to vessel walls during CSF handling

12. Hansson O, et al. Alzheimers Dement (Amst) 12(1):e12137 (2020). https://doi.org/10.1002/dad2.12137

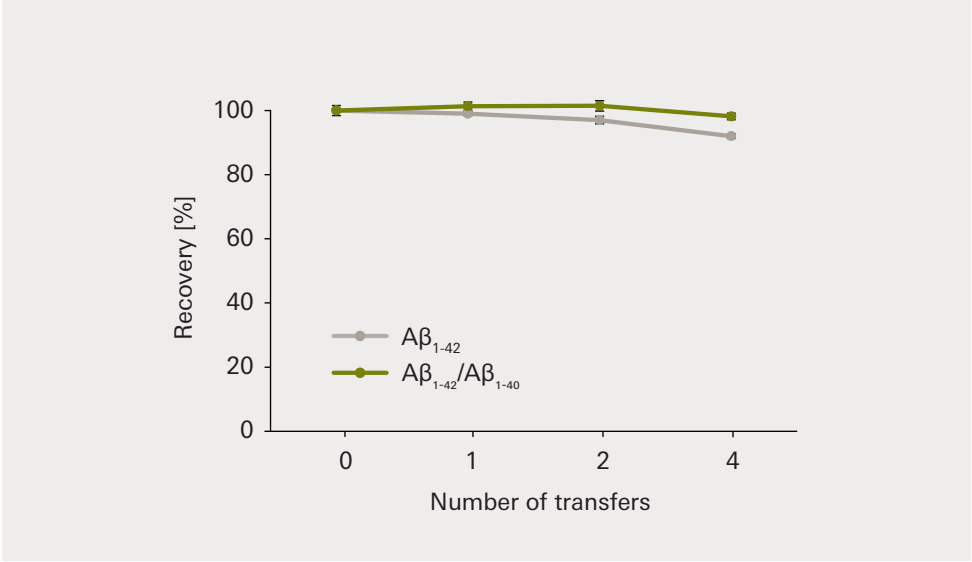
In the laboratory

Aliquotting of samples

Minimise the number of sample transfers

The adsorption of $A\beta_{1-42}$ is a repetitive process, which takes place every time a sample comes into contact with a new surface, for example after it is transferred to another tube. In a study with an aliquot volume of 1000 µl (50 % fill amount of tube), a reduction of around 5 % $A\beta_{1-42}$ after every transfer was observed. Around half of this loss occurred in the pipette tip.[10]

► The $A\beta_{1-42}/A\beta_{1-40}$ ratio remains constant regardless of transfers.



Measurable beta-amyloid quantity depending on the number of sample transfers (modified from Willemse et al., 2017)

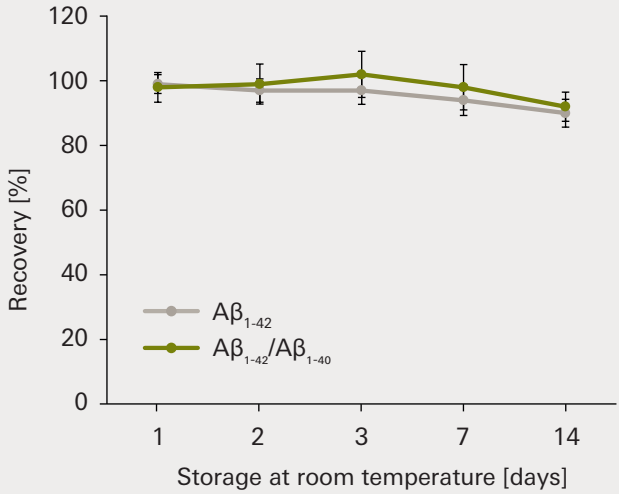
10. Willemse E, et al. Alzheimers Dement 13(8):885-892 (2017). http://doi.org/10.1016/j.jalz.2017.01.010

In the laboratory

Correct storage: temperature

More stable concentrations at lower temperatures

Depending on the length of time samples are stored between collection and analysis, storage at room temperature has a negative effect on the measurable beta-amyloid concentration in the CSF samples. In an uncooled state, for example, the measured $A\beta_{1-42}$ level decreased by about 6% after a week and by about 10% after two weeks. Overall the beta-amyloid concentrations were stable within a time frame of 72 hours at room temperature, one week at +4°C and two weeks at -20°C and -80°C (95–105% of the starting value).[11]



Measurable beta-amyloid quantity with storage at room temperature 1, 2, 3, 7 and 14 days after sample collection (modified from Janelidze et al., 2019)

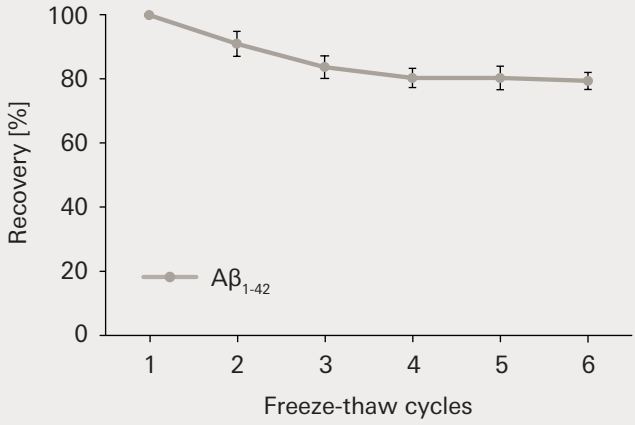
11. Janelidze S, et al. Alzheimers Res Ther 11(1):63 (2019). https://doi.org/10.1186/s13195-019-0517-9

In the laboratory

Correct storage: freeze-thaw cycles

Avoid repeated freeze-thaw cycles

The impact of freeze-thaw cycles on the measurable $A\beta_{1\text{-}42}$ quantity was demonstrated in a study. While the one-time freezing of CSF after sample collection up to analysis made no difference to the measured concentration of $A\beta_{1\text{-}42}$, the value dropped by 20% after three further freeze-thaw cycles. Additional freezing and thawing did not signifiantly reduce the beta-amyloid quantity any further.[13]



Impact of freeze-thaw cycles on the measurable beta-amyloid quantity (modified from Schoonenboom et al., 2005)

13. Schoonenboom NS, et al. Clin Chem 51(1):189-95 (2005). https://doi.org/10.1373/clinchem.2004.039735

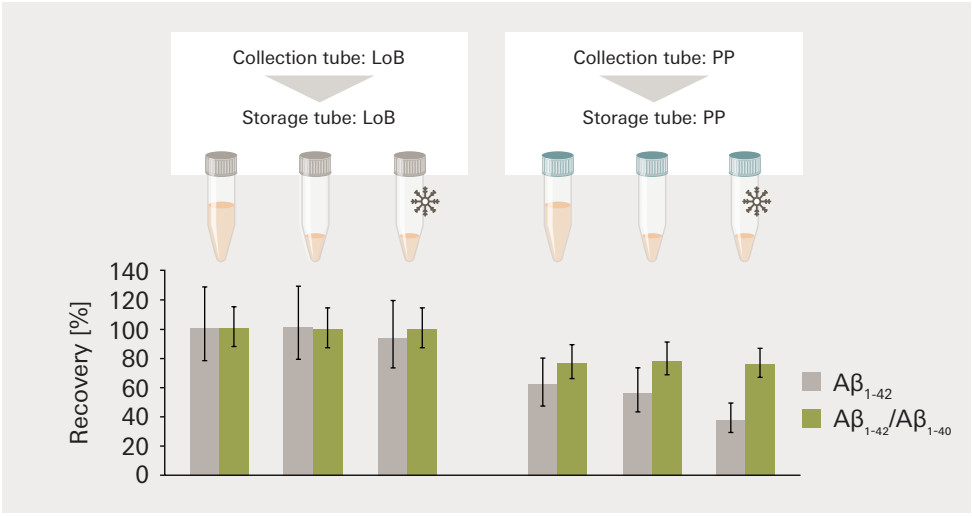
In the laboratory

Additive effects of preanalytical factors

Better recovery with LoB tubes

The cumulative effect of different preanalytical factors on the measurable beta-amyloid concentration was investigated in an analysis. Various combinations of factors were tested. The use of PP tubes for sample collection and storage led to much lower concentrations compared to the use of LoB tubes. A lower percental fill amount and an additional freeze-thaw cycle led especially in PP tubes to a further substantial reduction in the measurable beta-amyloid quantity.[9]

► The $A\beta_{1-42}/A\beta_{1-40}$ ratio was overall much more stable than the $A\beta_{1-42}$ measurement.



Impact of different combinations of tube material (PP vs. LoB), fill amount (40% vs. 13%) and number of freeze-thaw cycles (one vs. two) on the measurable beta-amyloid quantity (modified from Vanderstichele et al., 2016)

9. Vanderstichele H, et al. J Alzheimers Dis 53(3):1121-32 (2016). https://doi.org/10.3233/JAD-160286

Sample handling

Standard operating procedure (SOP)

Consensus article for preanalytics in Alzheimer's diagnostics, 2012 [14]

Consensus from the ABSI on the impact of preanalytical factors on the concentrations of $A\beta_{1\text{-}42}$, total tau and pTau(181) in CSF and detailed recommendations, including tube types, storage temperature and storage duration for CSF samples

Review of the current recommendations for preanalytics in dementia diagnostics, 2012 [15]

Comprehensive article combining the contents of two consensus protocols[14,16] with new knowledge to produce recommendations for standardised working procedures in preanalytics in dementia diagnostics

Protocol for preanalytics in the context of the analysis of Alzheimer biomarkers, 2020 [12]

Simplified, standardised protocol for the handling of fresh CSF samples prior to measurement of Alzheimer biomarkers for implementation in the clinical routine

To ensure reproducible results, it is recommended that every laboratory establish a standard procedure for handling CSF samples. This must apply already at sample collection and requires targeted communication with the clinicians submitting samples.

ABSI: Alzheimer's Biomarkers Standardization Initiative

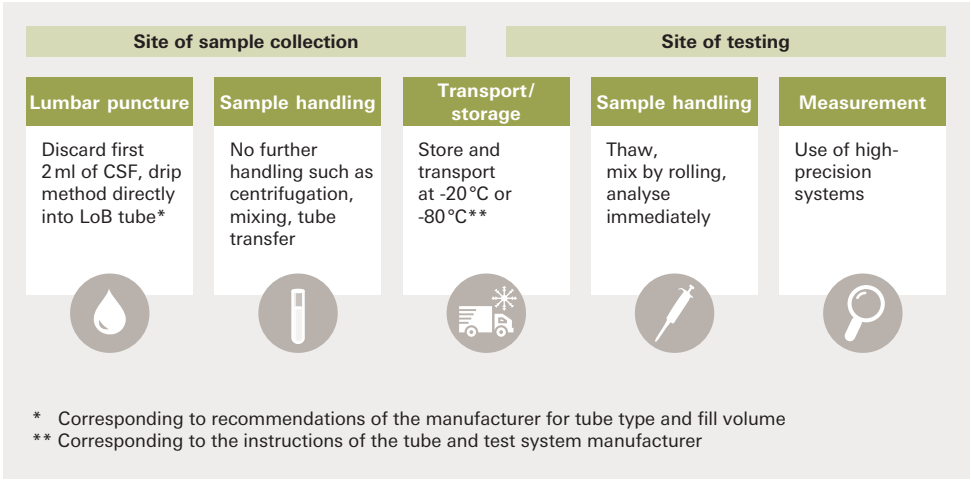
12. Hansson O, et al. Alzheimers Dement (Amst) 12(1):e12137 (2020). https://doi.org/10.1002/dad2.12137
14. Vanderstichele H, et al. Alzheimers Dement 8(1):65-73 (2012). https://doi.org/10.1016/j.jalz.2011.07.004
15. del Campo M, et al. Biomark Med 6(4):419-30 (2012). https://doi.org/10.2217/bmm.12.46
16. Teunissen CE, et al., Neurology 1;73(22):1914-22 (2009). https://doi.org/10.1212/WNL.0b013e3181c47cc2

Sample handling

Standard operating procedure (SOP)

International guideline for preanalytics in Alzheimer diagnostics, 2021 [17]

Published by the AA: guideline for the preanalytical handling of CSF samples in preparation for the detection of beta-amyloid and tau with the aim of reducing the variability of the measurement results. Encompasses hitherto existing recommendations in a unified protocol with a focus on routine procedures in specialised analytical laboratories.



Recommended preanalytical protocol for the collection, handling, storage and analysis of CSF samples that are frozen after the sample collection (modifiziert nach Hansson et al., 2021)

AA: Alzheimer's Association

17. Hansson O, et al. Alzheimers Dement 17(9):1575-1582 (2021). https://doi.org/10.1002/alz.12316

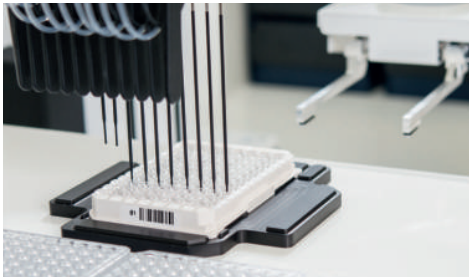
Internal quality control

Control material

To check the analysis results in relation to the measured analyte concentrations, control material with target values for the analytes is available:

Alzheimer CSF Control Set (EUROIMMUN product, order no.: CK 6500-0502-L)*

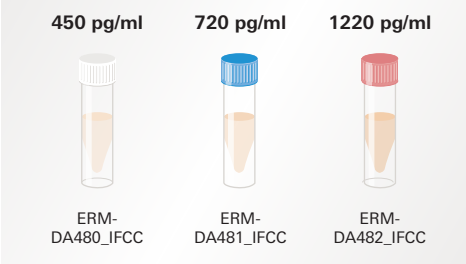
Five lyophilised CSF pools with target values for $A\beta_{1-42}$, $A\beta_{1-40}$, total tau and pTau(181) covering the complete measurement range of the corresponding EUROIMMUN ELISA. Only for use with ELISAs from EUROIMMUN.



Certified reference material (CRM) for beta-amyloid (1-42)

Established by the Global Biomarker Standardization Consortium (GBSC) of the Alzheimer's Association in collaboration with EUROIMMUN and commercially available via the Joint Research Centre of the European Commission.

https://crm.jrc.ec.europa.eu/?q=amyloid



* For research use only, not for in vitro diagnostics in the sense of EU Directive 98/79/EC

External quality control

Quality assessment schemes

INSTAND quality assessment: dementia markers (466)

The programme is aimed mostly at routine laboratories. Two schemes take place per year. A certificate is issued when the quality requirements are fulfilled. Five parameters for dementia diagnostics are available for quality assessment: $A\beta_{1-42}$, $A\beta_{1-40}$, $A\beta_{1-42}/A\beta_{1-40}$ ratio, total tau and pTau(181).

https://www.instand-ev.de/en/eqas/eqa-program/

INSTAND

CERTIFICATE

Survey of 29 July 2020

You have fulfilled the requirements of the External Quality Assessment with the following analysis

Cerebrospinal Fluid Analysis 06 - Dementia Markers (466):

Validity 12 months:

Amyloid β Peptid 42 (Aβ42)
Amyloid β Peptid 42 (Aβ42) - diagnostic comment
Total Tau Protein (Tau)
Total Tau Protein (Tau) - diagnostic comment
PhosphoTau Protein (pTau)
PhosphoTau Protein (pTau) - diagnostic comment
Amyloid β Peptid 40 (Aβ40)

Alzheimer's Association QC

The programme, which was started in 2009, is aimed mainly at academic laboratories. Participation is free of charge and no certificate is issued. The programme is offered for the dementia diagnostic parameters $A\beta_{1-42}$, $A\beta_{1-40}$, $A\beta_{1-42}/A\beta_{1-40}$ ratio, total tau and pTau(181) as well as the neurodegeneration marker NfL (neurofilament light).

https://www.gu.se/en/neuroscience-physiology/the-alzheimers-association-qc-program-for-csf-and-blood-biomarkers

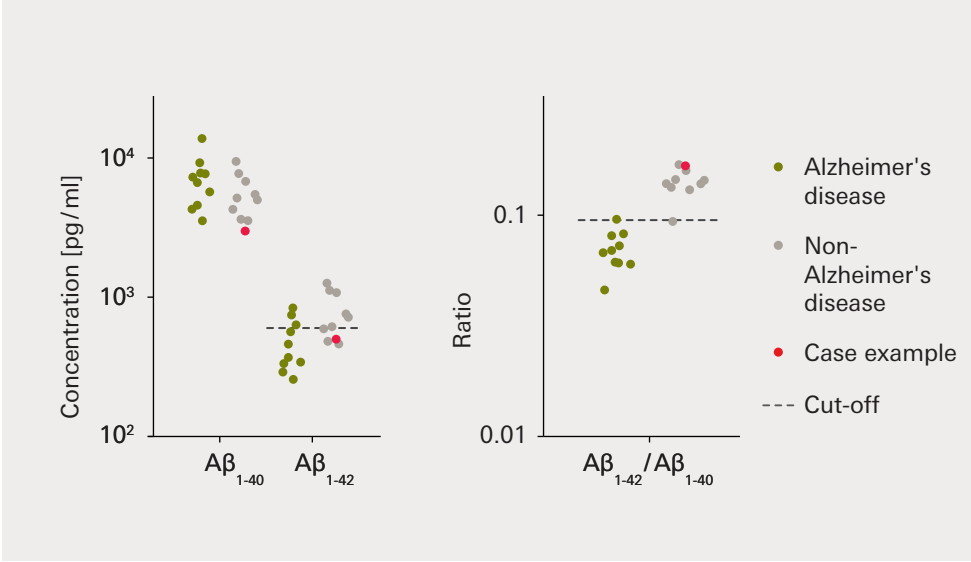
Results

The superior biomarker

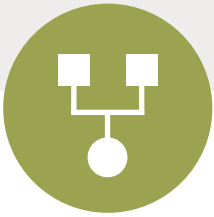
Determining the $A\beta_{1-42}/A\beta_{1-40}$ ratio can increase the efficiency of early diagnostics

In the ratio, $A\beta_{1-40}$ provides a measure of the individual beta amyloid expression and remains unchanged in Alzeimer's disease. The case example shows the CSF of a patient who shows comparatively low beta-amyloid concentrations due to a low basal expression or due to the impact of preanalytical factors. The patient cannot be clearly classified by measurement of $A\beta_{1-42}$ alone, but only through determination of the ratio. [18]

► Studies have also shown that diagnoses based on the $A\beta_{1-42}/A\beta_{1-40}$ ratio correlate better with amyloid-PET results than those based on the $A\beta_{1-42}$ concentration alone.[19]



18. EUROIMMUN. Internal data.
19. Janelidze S, et al. Ann Clin Transl Neurol 3(3):154-65 (2016). https://doi.org/10.1002/acn3.274



Results

Interpretation algorithms

Various algorithms have been developed for the diagnostic evaluation of dementia biomarkers, which up until now are not binding. Independent of the interpretation algorithm used, a diagnosis is not possible using laboratory parameters alone and should only be made when dementia syndrome is present and taking into account all clinical and diagnostic results.

PLM_R scale [20, 21]

The concentrations of the three CSF biomarkers $A\beta_{1-42}/A\beta_{1-40}$ ratio, total tau and pTau(181) are evaluated using a 3-point system. 0 stands for a normal profile, 1 corresponds to one abnormal and two normal analysis results, etc. The higher the evaluation is, the higher the probability of Alzheimer's disease.

Erlangen Score [22, 23, 24]

The results of beta-amyloid ($A\beta_{1-40}$ and $A\beta_{1-42}/A\beta_{1-40}$ ratio) and tau analyses (total tau and pTau(181)) are assessed in combination and evaluated using a scale from 0 to 4 – depending on the degree of deviation from the normal value. 0 stands for values in the normal range, 4 for pathological values in both biomarker groups and therefore probable Alzheimer's disease.

ATN system [25,26]

The relevant biomarkers are divided into three categories based on the type of pathophysiology that each reflects: amyloid pathology (A) determined by amyloid PET or CSF $A\beta_{1-42}$, tauopathy (T) established using tau PET or pTau in CSF, and neurodegeneration (N) determined by [18F]-fluorodesoxyglucose PET, MRT or total tau in CSF. Each category is evaluated as positive or negative. Suggested interpretations are derived from the different ATN profiles. The algorithm serves as a framework for research.

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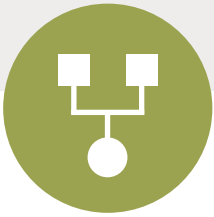

Results

Interpretation algorithms

IWG recommendations, 2021 [27]

Recommendations for a clinical-biological diagnosis of Alzheimer's disease in the diagnostic routine. A diagnosis of Alzheimer's is limited to persons who are biomarker positive and show specific Alzheimer phenotyes. Biomarker-positive but cognitively unimpaired persons, in contrast, are classified in the risk group for progression to Alzheimer's disease.

Publication on the harmonisation of clinical reporting, 2021 [28]

Recommendations for uniform terminology in reporting biochemical biomarkers to harmonise clinical reporting in Alzheimer's disease diagnostics. The formulations were developed on the basis of (pre-)analytical protocols and sample reports from 40 analysis centres worldwide.

amy-loid	total-Tau	pTau (181)	Consensus comments
N	N	N	Biochemical profile not consistent with Alzheimer's disease.
P	P	P	Biochemical profile consistent with Alzheimer's disease.
P	N	N	Biochemical profile consistent with an amyloidopathy.
N	P	N	Biochemical profile not consistent with Alzheimer's disease; may be consistent with other neurodegenerative disease and/or neuronal damage. (If t-tau is close to/above upper limit of detection with a high t-tau/p-tau[181] ratio, the profile may indicate Creutzfeldt-Jakob disease).
P	P	N	Atypical biochemical profile; may be consistent with Alzheimer's disease.
P	N	P	Atypical biochemical profile; consistent with Alzheimer's disease.
N	P	P	Atypical biochemical profile; not consistent with Alzheimer's disease.
N	N	P	Atypical biochemical profile; not consistent with Alzheimer's disease.
Note to be added to all comments: This biochemical profile must be interpreted in its clinical context and in conjunction with a physician.			

Summary of consensus comments for interpretation of biochemical profiles of Alzheimer's disease biomarkers in CSF (Delaby et al., 2021) N: normal; P: pathological

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Suitable tubes

The use of suitable tubes is the most important aspect of reliable analytics since unsuitable tube types can lead to incorrect diagnoses.

Examples of suitable tubes for Alzheimer's CSF diagnostics*

Manu-facturer	Sarstedt	Sarstedt	Sarstedt	Sarstedt	Eppendorf	Eppendorf	Sarstedt
Tube type	False bottom tube	False bottom tube	Screw-cap microtube	Screw-cap microtube	Conical centrifuge tube	Conical centrifuge tube	Round base tube
Cap type	Screw cap	Screw cap	Screw cap	Screw cap	Screw cap	Screw cap	Screw cap
Tube material	LoB	PP	LoB	PP	LoB	LoB	PP
Cap material	LoB	PP	HDPE**	PP	HDPE**	HDPE**	HDPE**
Volume, ml	2.5	2.5	2	2	5	15	10
Dimensions (L x Ø), mm	75 x 13	75 x 13	44 x 10.8	44 x 10.8	66.1 x 15.5	119.4 x 15.5	92 x 15.3
Order no.	63.614.625	60.614.011	72.703.600	72.694.006	0030 112 356	0030 112 216	62.610.201

* Only a selection of suitable tubes is shown. EUROIMMUN accepts no liability for the currentness, correctness and completeness of the information provided.

** Materials other than PP or LoB may have adverse effects on measurable beta-amyloid concentrations.

False bottom tubes are ideally suited for sample collection due to their low volume with at the same time large diameter (less contact surface).

Impact of the tube (p. 7)

Notes

EUROIMMUN test systems for the analysis of dementia markers in CSF

Parameter	Description	Test system	Order no.
Beta-amyloid (1-40)	Marker for individual amyloid expression. Beta-amyloid 1-42)/(1-40) ratio as a more precise marker to support diagnosis of amyloid pathology (Alzheimer's disease)	ELISA	EQ 6511-9601-L
Beta-amyloid (1-42)	Marker to support diagnosis of amyloid pathology (Alzheimer's disease)	ELISA	EQ 6521-9601-L
Total Tau	Marker to support diagnosis of neurodegeneration	ELISA	EQ 6531-9601-L
pTau(181)	Marker to support diagnosis of tauopathy	ELISA	EQ 6591-9601-L

Further products (for research use only*)

Product	Description	Order no.
Alzheimer CSF Control Set	CSF sample set with target values for beta-amyloid (1-40) and (1-42) as well as for total tau and pTau(181). Helpful for training and regular internal quality control of amyloid and tau measurements	CK 6500-0502-L

* For research use only, not for in vitro diagnostics in the sense of EU Directive 98/79/EC