



Alzheimer's Diagnosis Dilemma:

How Do You Confirm the Presence of Amyloid?

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INTRODUCTION

Otto (73 years old) is experiencing mild cognitive impairment (MCI).
How would you confirm amyloid pathology?

A clinical diagnosis based on cognitive symptoms alone can be unreliable in diagnosing AD.¹

In a primary care setting, a clinical diagnosis of AD was **inaccurate in 39% of patients**.¹

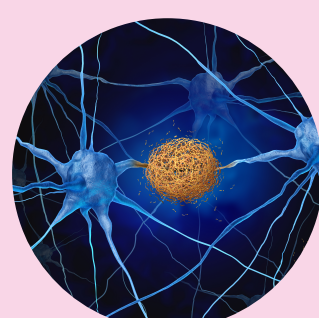
Delays in achieving a diagnosis can delay care and risk progression of the disease.²



39%
of patients are **inaccurately diagnosed**¹

Hallmarks of Alzheimer's disease include:^{2,4}

- accumulation of β -amyloid protein outside neurons
- twisted strands of tau protein inside neurons
- inflammation and atrophy of brain tissue



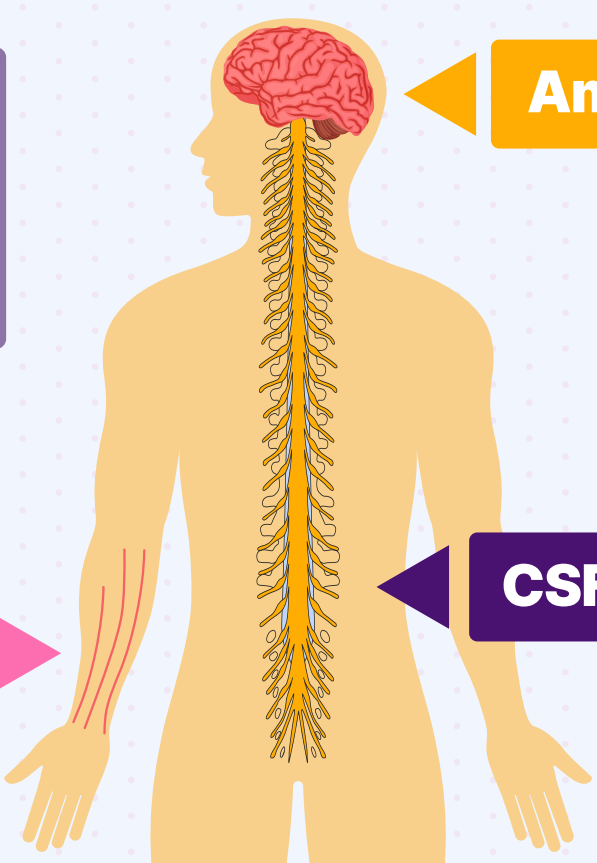
How can we confirm amyloid pathology?

95%* of patients want simple testing if they are symptomatic,² and confirmation is becoming increasingly necessary for treatment of AD or enrollment into clinical trials.^{1,3,4}

Amyloid PET Imaging

Blood-based biomarkers (BBBMs)

CSF Biomarkers

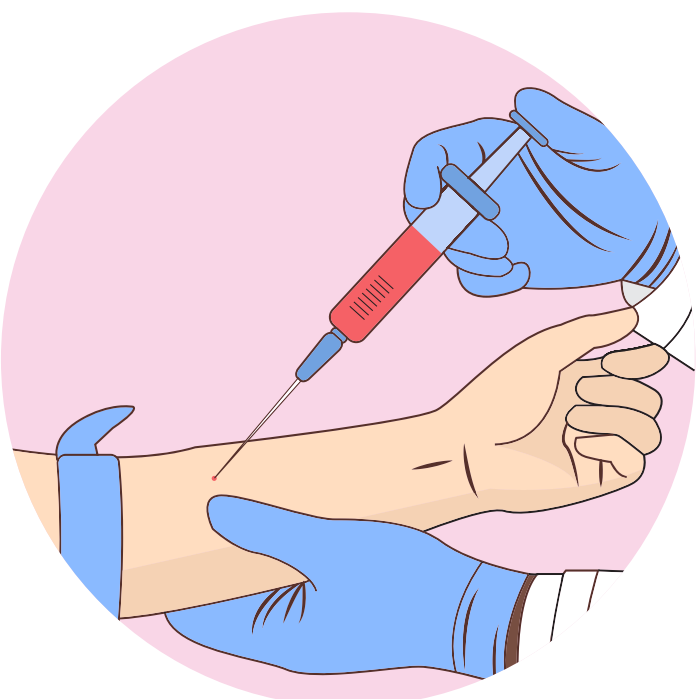


BBBMs

Blood testing allows amyloid status evaluation using plasma markers.^{1,6}

Several studies have suggested that plasma ptau217 and the ptau217/A β 42 ratio could have sufficient accuracy for use in symptomatic patients.^{7,8}

As Otto is symptomatic, he may be able to undergo a minimally invasive blood test to assess his amyloid status. BBBMs have recently been cleared by the FDA for use in symptomatic patients, making this an emerging tool for use in clinical practice.



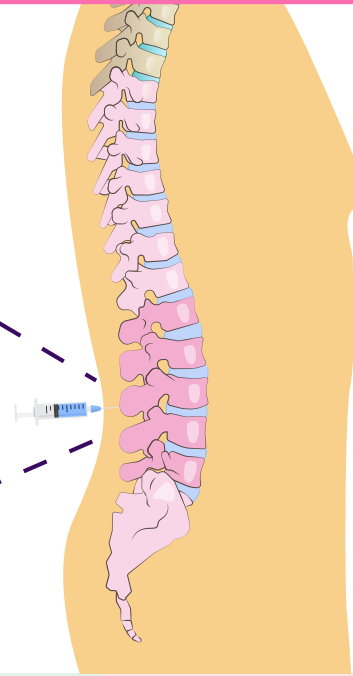
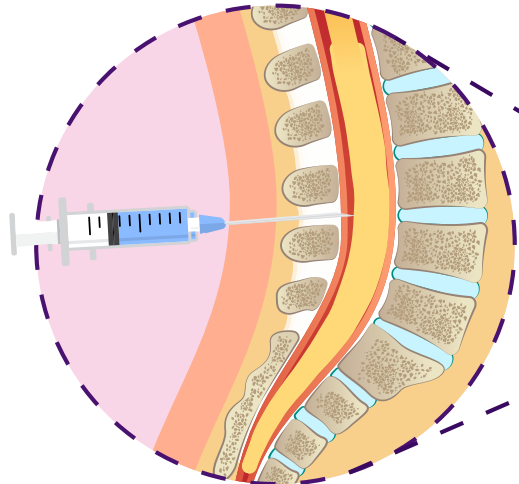
Strengths

- Accuracy >90%; comparable to CSF ratios.^{1,7}
- Minimally-invasive, accessible, and scalable.⁷
- ptau217/A β 42 ratio has recently been FDA cleared for use in symptomatic patients.⁹
- Endorsed by the 2024 Alzheimers Association Workgroup.³

Limitations

- Approved for use only in patients with symptoms, not in the cognitively unimpaired.⁷
- Limited real-world experience and clinician familiarity.^{3,7}
- Potential for intermediate results.⁷
- Intended for use by specialists.⁷

CSF Biomarkers



Otto suffers from both diabetes and hypertension, so his CSF biomarker results may potentially be influenced by these comorbidities.^{4,6}

Strengths

- Hybrid ratios of analytes have sensitivity and specificity >90%.⁴
- FDA approved and 2024 guideline endorsed.⁵
- Measures multiple analytes that can expand the assessment of cognitive impairment.⁴
- Broadly available and relatively low cost.⁴

Limitations

- Invasive procedure.⁴
- Requires a highly trained clinician.⁴
- Results can be influenced by comorbidities.^{4,5}

Amyloid PET Imaging



Otto lives in a rural area, where PET scans may not be widely available, he may have to travel a long distance to undergo amyloid PET imaging.

One study found that the mean one way travel time to a PET facility was 69 minutes.¹⁰

Strengths

- Sensitivity and specificity >90% for AD pathology.⁴
- FDA approved and 2024 guideline endorsed.⁵
- Minimally invasive.⁴
- Validated versus post-mortem pathology.⁴

Limitations

- Limited availability.⁴
- Involves radiation exposure.⁴
- Does not assess other causes of cognitive impairment.⁴
- Subject to inter-rater variability.⁴

KEY TAKEAWAYS

The majority of patients with Alzheimer's disease want a simple diagnostic test.²

Current and future disease modifying therapies for AD require confirmation of amyloid for initiation of therapy.^{1,5}

Ultimately, the diagnostic approach should be selected based on the individual patient and clinical context.⁴



*A survey of 1,702 U.S. adults aged 45 years and older conducted from November 7–18, 2024, by the Alzheimer's Association.²

Abbreviations

A β : amyloid beta; AD: Alzheimer's disease; BBBM: blood-based biomarker; CSF: cerebrospinal fluid; MCI: mild cognitive impairment.

References

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