ECHO IDAHO

Alzheimer's Disease and Related Dementias

Blood-based Biomarkers for Alzheimer's Disease

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None of the planners or presenters for this educational activity have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

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Financial disclosures

I have no relevant financial relationships to disclose.

I do intend to discuss off-label use of blood-based biomarkers for Alzheimer's disease.

Learning objectives

Describe blood-based biomarkers closest to routine clinical implementation in diagnosis and management of Alzheimer's Disease.

Discuss the limitations of blood-based biomarkers for Alzheimer's disease.

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Take home points

There is no single, stand-alone test to diagnose Alzheimer's Disease today!

Blood-based biomarker testing is one piece in the diagnostic process and should appear much later in the process.

Dementia specialists should be the only ones ordering biomarker tests.

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Recommended podcast

GeriPal 2/6/25. How to make an Alzheimer's Diagnosis in Primary Care: A podcast with Nathaniel Chin. Hosted by Geriatricians Dr. Eric Widera and Alex Smith. UCSF.

- This podcast is relevant because it talks about how blood-based biomarkers are already changing how we approach diagnosis of Alzheimer's Disease.

Landmark study in primary care

Ptau-217 / nonPtau-217 ratio combined with Amyloid42/40 ratio in plasma had diagnostic accuracy of 90% in detecting AD pathology (as defined by CSF biomarker positivity) in primary care and specialty clinics.

Dementia specialists' accuracy: 73%

PCP accuracy: 61%

- Palmquist et al. JAMA July 28, 2024

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Diagnostic process: Practice guidelines

Diagnostic process involves 8-14 components: consent, history, exam, cognitive testing, functional assessment, initial workup, identifying potentially modifiable factors, brain imaging, diagnostic disclosure and in as necessary, specialty referral, neuropsychological testing, genetic testing, advanced diagnostic testing, molecular imaging, FDA-approved AD biomarker testing.

- Atri et al. Alzheimer's Association clinical practice guideline for the Diagnostic Evaluation, Testing, Counseling, and Disclosure of Suspected Alzheimer's Disease and Related Disorders (DETeCD-ADRD): Executive summary of recommendations for primary care. Alzheimer's & Dementia 2024.

Case

88-year-old patient clinically diagnosed with moderate AD dementia

His 63-year-old son with “lot of forgetfulness.”

38-year-old grandson worried about developing AD in the future

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Current landscape on biomarkers for AD

No blood-based biomarkers are currently FDA approved.

CSF-based biomarkers are FDA approved.

Amyloid PET scan is FDA approved.

A/T/N Classification

Amyloid positive (and corresponding biomarkers)

Tau positive (and corresponding biomarkers)

Neurodegeneration positive (and corresponding biomarkers)

- Jack et al. A/T/N: An unbiased descriptive classification scheme for Alzheimer's disease biomarkers. Neurology 2016.

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Blood / Plasma Biomarkers

Plasma A-beta42/40 (reduced in AD) and Phospho-tau levels (elevated in AD)

Neurofilament light chain (NFL) (elevated if there is neurodegeneration)

Glial Fibrillary Acidic Protein (GFAB) (elevated if there is neurodegeneration)

- Johannson C et al. Plasma biomarker profiles in Autosomal Dominant Alzheimer's Disease. Brain 2023; 146:1132-1140.

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CSF AD biomarkers over 20 years

A-beta 42 – 18 years before diagnosis of dementia

A-beta 42 / 40 ratio – 14 years earlier

Phospho Tau 181 – 11 years earlier

Total Tau – 10 years earlier

Neurofilament light chain – 9 years earlier

Hippocampal volume – 8 years earlier

Cognitive decline – 6 years earlier

- Jia et al. Biomarker Changes during the 20 Years Preceding Alzheimer's Disease. NEJM 2024.

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Phospho Tau 217

Blood based Phospho Tau 217 was clinically equivalent to or superior to the FDA-approved clinically available CSF biomarkers for Alzheimer's Disease

- Barthelemy et al. Highly Accurate Blood Test for Alzheimer's Disease Comparable or Superior to Clinical CSF Tests. Nature Medicine 2024.

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Clinical recommendations for blood-based biomarkers

Recommend against individuals getting their tests done (DIY testing / direct to consumer testing / getting a provider to order the test)

If tests are done, they should be interpreted by dementia experts in the context of a thorough assessment

- Mielke et al. Recommendations for clinical implementation of blood-based biomarkers for Alzheimer's disease. Alzheimer's & Dementia July 2024

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Clinical recommendations for blood-based biomarkers

Tests should not be done in asymptomatic individuals and individuals with subjective cognitive decline

Many individuals with MCI and AD-dementia may benefit from these tests

- Mielke et al. Recommendations for clinical implementation of blood-based biomarkers for Alzheimer's disease. Alzheimer's & Dementia July 2024

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Diversity and Inclusion

Blood-based biomarkers have not been adequately studied in Blacks, Hispanics, Indigenous people and other minority groups.

Limitations

Comprehensive and up-to-date overview of blood-based biomarkers including appropriate use criteria are currently not available.

- Varesi et al. Blood-Based Biomarkers for Alzheimer's Disease Diagnosis and Progression: An Overview. Cells 2022.

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Risks of disclosure of biomarker results

Emotional distress significantly higher in cognitively symptomatic individuals than asymptomatic individuals.

- Kim et al. Emotional distress following amyloid PET result disclosure: Heightened among those with cognitive symptoms. Alzheimers & Dementia 2025.

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Ethical considerations

Blood-based biomarker tests for AD may do more harm than good?

Future

Blood-based biomarkers may enable accurate earlier and faster diagnoses as well as aid in risk assessment, early detection, prognosis, and management.

- Hampel et al. Blood-based biomarkers for Alzheimer's disease: Current state and future use in a transformed global healthcare landscape. Neuron 2023.

THANK YOU

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