# Clinical Medicine Today

**Alzheimer's: Can a new blood test pave the way for earlier detection of the disease?**

Alzheimer's disease, a debilitating form of dementia, impacts an estimated 55 million people globally. The societal impacts of the disease can be profound, with family members having to make personal and financial sacrifices in order to care for their loved ones. Currently there is no cure for Alzheimer's; and treatments focus on delaying the progression of the disease and alleviating symptoms.

In 2024, Swedish researchers made headlines by developing a blood test with an impressive 90% accuracy in diagnosing Alzheimer's [1]. This important finding might allow for earlier diagnosis and therefore better outcomes in these patients.

A significant challenge in Alzheimer's management is accurately diagnosing the condition. Clinical scores from the STROBE & STARD checklists typically have a diagnostic accuracy of 60-70%. As a result, Alzheimer's disease can often only be confirmed post-mortem. The new blood-based test could become a game changer in the field.
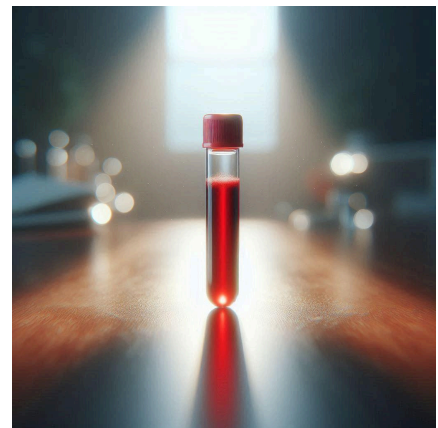
The marker, a serum protein called p-tau217, becomes elevated in people developing Alzheimer's disease. P-tau217 is a variation of the tau proteins responsible for maintaining the functionality of neurons in the healthy brain. Tau stabilizes microtubules in the brain allowing nutrients to be transported within the functioning neurons. It allows the brain to work.
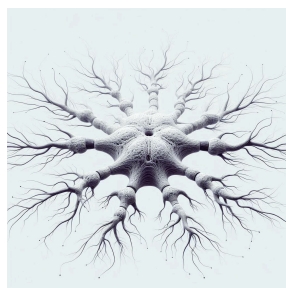
As we age, these proteins can become modified by phosphorylation - for those interested p-tau217 stands for *phosphorylated tau at position* 217 in the protein sequence. Phosphorylated tau can't function as well as the healthy form of the protein. It has been implicated in the formation of tau tangles, aggregates which clog up the neurons and impair brain function. Researchers currently believe that this is a necessary initial step for Alzheimer's disease to develop.

The test involves comparing the ratio of p-tau217 with all the tau proteins in the blood. The tau ratio, when combined with beta-amyloid ratios, is rolled into an aggregated score called the amyloid probability score 2 (APS2). Beta amyloid peptides are the other potential culprit in the development of Alzheimers. The 42 amino acid version of the peptide forms plaques in the brain, whilst the shorter 40 amino acid version does not. Amyloid plaques are associated with a number of types of dementia, including Alzheimer's.

The good news is that the APS2 score from blood samples correlated well with the same markers found in cerebrospinal fluid. This makes the test clinically viable as blood draws are cheaper, easier and more popular than lumbar punctures.

The Swedish blood test could bring the therapeutic window forward in the progression of the disease, and may well result in better outcomes for patients.

There are currently a number of Alzheimer therapies which could benefit from this test. These range from cholinesterase inhibitors such as Aricept (donepezil) and Exelon (rivastigmine) to glutamate receptor agonists such as Namenda (memantine). Additionally, within the last two years, immunotherapies - Leqembi (lecanemab) and Kisunla (donanemab), have been approved by the FDA which target the amyloid plaques building up in the Alzheimer brain.

The therapeutic future is even brighter, with promising antibody-drug conjugates like Gantenerumab and Crenezumab currently being tested in phase 3 clinical trials. Hematopoietic stem cells have been shown to be effective in animal models too, and are heading into human trials.

The p-tau217 protein and associated APS2 score could be an important leap forward in the fight against Alzheimer's disease. With its simplicity, affordability, and high accuracy, this diagnostic tool offers new hope for millions of individuals and their families. Accurate detection not only opens doors to more effective treatments, but also empowers patients with the knowledge and opportunity to make informed decisions about their future.

It couldn't come at a better time.

References

1. Palmqvist S, Tideman P, Mattsson-Carlgren N, et al. Blood Biomarkers to Detect Alzheimer Disease in Primary Care and Secondary Care. JAMA. 2024;332(15):1245–1257. doi:10.1001/jama.2024.13855

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