Blood Tests Detect Alzheimer's Disease Before Symptoms Start

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Diagnosing Alzheimer's disease before symptoms develop may soon be as simple as getting a blood test. New blood tests for certain biomarkers show promise, providing physicians an alternative to expensive scans or invasive spinal taps to make a diagnosis.

Key takeaways:

- The current tests used to diagnose Alzheimer's disease (brain scans and analysis of cerebrospinal fluid) are expensive and/or invasive.
- Alzheimer's disease can be diagnosed by identifying the presence of three biomarkers in bodily fluids, organs, or tissues: two proteins, tau tangles and beta-amyloids, and neurodegeneration of nerve cells in the brain.
- Three blood tests for Alzheimer's disease are commercially available, but they identify only two of the three biomarkers that must be present to make a diagnosis of Alzheimer's disease.
- BD-tau, a promising new blood test revealed at the end of 2022, detects not only evidence of two hallmark proteins in the blood of patients with Alzheimer's

disease, but also detects evidence of neurodegeneration specific to brain cells.

- Early detection of Alzheimer's disease allows you to make healthy lifestyle changes, develop a long-term plan of care, and participate in clinical trials for medications that may help slow the neurodegenerative process.

How to test for Alzheimer's disease

Until about twenty years ago, the only way to diagnose Alzheimer's disease was to do an autopsy and look at a person's brain after death. Researchers have now identified certain biomarkers in the blood and brains of people who develop various forms of dementia. Biomarkers can be a protein or other type of molecule that, when present in bodily fluids (cerebrospinal fluid, blood, or urine), organs or tissues, can be measured to identify whether a certain disease process is occurring.

Physicians are currently screening for Alzheimer's disease using **brain scans**, such as magnetic resonance imaging or amyloid positron emission tomography, or by **analyzing cerebrospinal fluid** gathered by doing a spinal tap. These tests **do not allow doctors to make a definitive diagnosis** of Alzheimer's disease, as they do not identify the three types of evidence required under guidelines developed by the National Institute on Aging (NIA) and the

Alzheimer's Association. Another downside is that these tests are costly and/or invasive.

More recently, researchers have been working to develop simple blood tests to identify certain biomarkers or proteins in the blood that indicate that you are at risk for developing Alzheimer's disease.

Biomarkers of Alzheimer's disease

In 2011, the NIA and the Alzheimer's Association created guidelines to diagnose Alzheimer's Disease known as the AT(N) Framework. These guidelines require the identification of three biomarkers or indicators of Alzheimer's disease before a definitive diagnosis can be made. These biomarkers include evidence of:

- **Tau tangles**. Abnormal proteins that stick together and become twisted inside brain nerve cells. These tangles block the transportation of nutrients and communications throughout these nerve cells.
- **Amyloid plaques.** Proteins (amyloid beta) that stick together and clump in the spaces between nerve cells, causing them to die.
- **Neurodegeneration**. Death of nerve cells in the brain.

Which blood tests show Alzheimer's disease:

Researchers have been working to develop blood tests that can identify the three classic biomarkers of Alzheimer's disease before you show symptoms of Alzheimer's, such as memory loss, issues with reasoning, or problems with speech.

As of September 2022, there were three types of Alzheimer's blood tests available commercially. These commercially available blood tests identify abnormal levels of amyloid beta and tau, two of the three biomarkers required by the AT(N) Framework to be present for a definitive diagnosis of Alzheimer's disease. However, these tests do not meet the third requirement of the AT(N) Framework, as they cannot detect evidence of neurodegeneration or death of nerve cells specific to the brain.

The three commercially available tests identify either the tau or beta-amyloid proteins in your blood as indicators that you may be at risk of developing Alzheimer's disease. The tests have been certified for clinical use in the United States, but are not FDA approved. Medicare and Medicaid do not cover the cost of these tests because they are not FDA approved. These tests include:

PrecivityAD

This test was developed by C2N diagnostics. The test examines the ratio of beta-amyloid proteins and determines if you carry the APOE4 gene, which are indicators that you are at increased risk of developing Alzheimer's disease.

Available since 2020, the test can be ordered by physicians through the manufacturer's website in 49 states, the District of Columbia, and Puerto Rico. The test costs over $500 and is not covered by insurance.

Quest AD-Detect

Introduced by Quest Diagnostics, this blood test also measures beta-amyloid proteins in your blood to determine your risk for developing Alzheimer's disease. It does not determine if you have any genetic biomarker for the disease.

The test became available in May 2022, with a cost of $500. There is limited coverage by some health plans.

Simoa pTau-181 assay

Developed by Quanterix and brought to the market in late July, 2022, this blood test measures tau protein, p-tau181. Research has revealed that the higher the p-tau181 level in the blood, the more likely you are to develop beta-amyloid plaques that clump between and result in death of brain nerve cells. This is one of the indicators of Alzheimer's disease.

The test can be ordered by a physician through the manufacturer website and is not covered by insurance. There is some evidence that this test may not be accurate in the Black population.

The Alzheimer's Association is optimistic regarding further development of blood testing; however, they recommend using these current

tests cautiously and in conjunction with brain scans or cerebrospinal fluid testing.

New biomarker for Alzheimer's disease

Brain-derived tau, or BD-tau, is a new biomarker identified by neuroscientists at the University of Pennsylvania School of Medicine and University of Gothenburg, Sweden at the end of 2022. BD-tau is a **protein that maintains the structure of nerve cells.** Measuring this biomarker is **believed to be more accurate** than the proteins measured in other blood tests. The new BD-tau blood test selectively detects specifically BD-tau, instead of other tau type proteins produced by cells outside of the brain. This is important because the test meets the AT(N) Framework requirement that the test must detect biomarkers which specifically identify the death of nerve cells in the brain.

The BD-tau blood test is very promising. Larger scale clinical validation of this blood test will need to be conducted before it is commercially available for day-to-day clinical use in diagnosing Alzheimer's disease.

Blood test benefits for Alzheimer's disease

There is currently **no way to stop or reverse the damage** done to the brain by Alzheimer's disease. It is hoped that minimally invasive blood tests will **provide a method of routine**

screening for Alzheimer's disease before memory, cognitive, or behavioral symptoms develop. If a simple blood test allows you to detect Alzheimer's disease early, you will be able to implement a healthy lifestyle to try to slow the decline of cognitive ability and other devastating symptoms.

Early detection through blood testing will also allow more time to:

- Accomplish bucket list trips or family activities before symptoms develop or worsen.
- Create a plan of how and where you want to be cared for.
- Establish a legal decision-maker and set aside finances to pay for the implementation of a plan of care.

Lastly, from a research perspective, the development of reliable blood tests for Alzheimer's disease will allow those who have not developed symptoms to be included in clinical trials that are exploring new medications or other treatments to slow the progression of the disease.

Evidence of neurodegeneration in the brain is one of the three components of the AT(N) Framework required to establish a diagnosis of Alzheimer's disease. One significant limitation of the three blood tests that are commercially available has been that they cannot identify evidence of the death of brain nerve cells. With the discovery of a new blood biomarker, BD-tau, there is hope that blood tests will be able to

definitively diagnose Alzheimer's disease before symptoms become obvious.

Although no one wants to be diagnosed with Alzheimer's disease, early detection will allow you to take more control over your diagnosis. Implementation of healthy lifestyle habits in the early stages may help slow the associated cognitive and behavioral decline. In addition, these blood tests may help you get enrolled in clinical trials for medications that may treat or help slow the development of devastating cognitive symptoms. Early detection will also give you more time to do things that are important to you and put financial and legal protections in place to ensure you are cared for in a way that preserves your dignity and quality of life.

Resources:

1. Blood Biomarkers from Research Use to Clinical Practice: What Must Be Done? A Report from the EU/US CTAD Task Force.
2. Brain-derived tau: a novel blood-based biomarker for Alzheimer's disease-type neurodegeneration.
3. The Alzheimer's Association appropriate use recommendations for blood biomarkers in Alzheimer's disease.
4. New Biomarker Test Can Detect Alzheimer's Neurodegeneration in Blood.
5. National Plan to Address Alzheimer's Disease: 2021 Update.

6. What Are Biomarkers and Why Are They Important? Transcript.