Biomarkers and Alzheimer's disease

What are biomarkers?

The term biomarker is short for "biological marker" and broadly refers to a medical sign or characteristic observed in living things. Biomarkers are measurable biological changes that can show if a disease is present or a person is at risk for developing a disease.

Scientists and health care professionals screen for certain diseases by detecting and measuring biomarkers. Some methods include conducting imaging scans, and collecting samples of bodily fluids like blood, saliva, urine and cerebrospinal fluid (a clear, colorless liquid that surrounds the brain and spinal cord). For instance, a high blood glucose (sugar) level is a biomarker of diabetes and is commonly used to diagnose the condition.

Are there biomarkers to detect Alzheimer's disease?

While physicians use a variety of tools to evaluate memory and thinking problems, an Alzheimer's diagnosis currently relies largely on observing cognitive decline — a point at which the disease has already damaged the brain. Researchers hope to discover accessible and accurate ways of detecting Alzheimer's disease that will allow for earlier diagnosis, so that treatments can be started before the onset of symptoms. Experts believe that biomarkers offer one of the most promising paths to Alzheimer's diagnosis, in conjunction with other testing.

Several potential biomarkers are being studied for their ability to indicate early stages of Alzheimer's — and a few are already used more widely today to screen for the disease. For example, two hallmark brain changes of Alzheimer's disease — the accumulation of protein fragments known as beta-amyloid and tau — are biomarkers that can be detected using imaging technologies or assessed through a cerebrospinal fluid test. However, the presence of these biomarkers alone is not sufficient to determine an Alzheimer's diagnosis.

While not all of the following tools are available in your doctor's office, researchers are hard at work on noninvasive, cost-effective and reliable testing methods to improve the diagnostic process for all individuals.

Brain imaging/neuroimaging

Imaging technology is regularly used today for early detection of Alzheimer's, and continues to evolve with promising new brain imaging techniques.

Structural imaging
Structural imaging provides information about the shape, position or volume of brain tissue. Structural techniques include **magnetic resonance imaging (MRI)** and **computed tomography (CT)**.

The brains of people living with Alzheimer's shrink significantly as the disease progresses. Structural imaging research has shown that shrinkage in specific brain regions such as the hippocampus may be an early sign of Alzheimer's.

Today, a standard workup for Alzheimer's or other dementia may include structural imaging. These tests are also used to rule out other conditions that may cause symptoms similar to Alzheimer's,

Functional imaging
Functional imaging technology is used to study human brain function and measure changes in the activity and processes within the brain, such as blood flow and cell metabolism. Functional imaging research suggests that those with Alzheimer's typically have reduced brain cell activity in certain regions. For example, studies with fluorodeoxyglucose (FDG)-positron emission tomography (PET) indicate that Alzheimer's is often associated with reduced use of glucose in brain areas important in memory, learning and problem-solving. FDG-PET may be covered by insurance for people with a recent diagnosis of dementia and documented cognitive decline of at least six months who meet diagnostic criteria for both Alzheimer’s and frontotemporal dementia.

Molecular imaging
Molecular imaging, which also uses PET scans, is among the most active areas of research aimed at finding new approaches to diagnose Alzheimer's in its earliest stages. Molecular strategies may detect biological clues of Alzheimer's before the disease changes the brain's structure or function, or takes an irreversible toll on memory, thinking and reasoning. Molecular imaging also may offer a new strategy to monitor disease progression and assess the effectiveness of next generation, disease-modifying treatments. Several molecular imaging compounds are being studied, and four have been approved by the FDA for clinical use:

- Florbetaben (Neuraceq®), Florbetapir (Amyvid®) and Flutemetamol (Vizamyl®) have been approved for detection of beta-amyloid in the brain.

- Flortaucipir F18 (Tauvid®) has been approved for detection of tau in the brain.

Cerebrospinal fluid (CSF) tests

CSF is a clear fluid that bathes and cushions the brain and spinal cord. Adults have about 1 pint of CSF, which physicians can sample through a minimally invasive procedure called a lumbar puncture, or spinal tap.

Research suggests that Alzheimer's disease in early stages may cause changes in the levels of biomarkers, like tau and beta-amyloid, found in cerebrospinal fluid. Another potential marker is neurofilament light (NfL), an increased level of which has been found in neurodegenerative diseases, but it is not specific to Alzheimer's.

CSF tests are currently used by dementia specialists to aid in the diagnosis of Alzheimer's, and research continues to develop and standardize new markers that will aid in diagnosis and detection of other dementias.

- One CSF Amyloid Ratio test, Lumipulse®, received FDA approval and is a new diagnostic tool that clinicians can use to detect amyloid in CSF, which can be predictive of amyloid changes in the brain.

Blood tests

Researchers are investigating whether consistent and measurable changes in levels of specific markers in the blood are associated with Alzheimer's. These markers may include tau, beta-amyloid or other biomarkers that can be measured before and after symptoms appear.

An urgent need exists for simple, inexpensive, noninvasive and easily available diagnostic tools such as blood tests to diagnose the disease.

Today, blood tests are already improving the design of clinical trials, and they are being used in some specialty care centers. In the future, they are very likely to revolutionize the diagnostic process for Alzheimer's and all other dementia.

There are a few blood tests currently on the market that can be ordered by health care providers to aid in the diagnosis of memory complaints. These tests do not yet have FDA approval. At this time, it is recommended that blood tests only be used by specialty care doctors who are seeing patients with memory complaints. They are not recommended for individuals who do not have any cognitive or memory symptoms.

The currently available tests may predict the presence of amyloid changes in the brain or the presence of neurodegenerative disease or neuronal damage. These blood tests cannot be used as a standalone test to diagnose Alzheimer's disease or any other dementia; they will be used as part of a diagnostic workup with other exams.

Emerging Biomarkers

Retinal Imaging

Some researchers think retinal imaging has the potential to detect biological signs of Alzheimer's disease within certain areas of the eye. Because of the eye's proximity to the brain and the similarity of certain changes observed in both, changes in the eye may correlate with neurodegeneration in the brain, damage to the blood vessels of the brain or other disease-associated processes.

If proven, retinal imaging could be an accurate, noninvasive and affordable option for diagnosis.

Saliva and Skin

Other emerging biomarkers include examining components in saliva and the skin for signals that may indicate early biological changes in the brain. Tests with these types of biomarkers are still very exploratory, and more research is needed before these tests or biomarkers can be used more routinely to study risk or aid in diagnosis.

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