Bob's LAST MARATHON
Living the Alzheimer's Journey

TRANSCRIPT

The Promise of Biomarkers

More and more, the term "biomarkers" is being used in the context of diagnosing and monitoring Alzheimer's disease and related disorders. But what does the term "biomarker" mean? In essence this is a biological feature of a disease that we can measure either through imaging, laboratory tests, or other kinds of recordings from the body. Let's use an example that most everyone can relate to. Say you go to the doctor complaining of shortness of breath and maybe a cough. Now, there are many illnesses that can cause these symptoms, and the treatment will vary accordingly. The causes might range from an upper respiratory viral infection to bacterial pneumonia to asthma, emphysema, heart failure, or cancer. The doctor can suspect some of these based on history or examination findings. But to be sure, she may order a variety of biomarker tests. These might include a chest X-ray, an electrocardiogram, a CT scan, or lab tests on blood or sputum and more. With these biomarker data, the physician can make an accurate diagnosis, recommend the right treatment, and follow whether a person is getting better or worse.

Now let's take the case of someone going to the doctor with memory decline. Based on symptoms of forgetfulness or word-finding difficulties, how long the symptoms have been present and the like, the doctor can suspect what might be causing the cognitive impairment. She might suspect Alzheimer's disease. However, she'll want to make sure other things that can cause cognitive decline aren't present, so she may order some common biomarker studies—a brain MRI scan or head CT scan to look for evidence of strokes, tumors, or fluid collections. She might order some blood tests to look for hypothyroidism or vitamin deficiencies. If all these tests come back negative, then her suspicion of Alzheimer's disease may be higher. These biomarkers rule out other causes of memory loss, but she still hasn't made a positive identification.

We used to say that the only way to be sure that Alzheimer's disease is the cause of someone's cognitive decline is if you look at someone's brain tissue under a microscope after they die and see the telltale amyloid plaques and tau tangles that define the disease. This would be a positive ID. What has transformed the field of Alzheimer's disease over the last two decades is the development of biomarkers using molecular neuroimaging, spinal fluid laboratory tests, and, most recently and importantly, blood tests that indicate the presence or absence of these brain amyloid plaques and tau tangles with a very high degree of certainty.

Let me briefly discuss the different types of biomarkers for Alzheimer's disease.

PET scans, or positron emission tomography, are a kind of brain imaging test that is now used to visualize the presence, absence, or amount of specific molecules in the brain. The most important kinds of PET scans used in Alzheimer's disease are glucose, amyloid, and tau PET scans. Glucose PET scans have been used for many years to look for patterns of metabolic activity in the brain. Amyloid PET scans are now approved for clinical use as well as research, although their cost is usually not covered by insurance. Tau PET scans are still for research use only.

The way PET scans work is that a radio-labeled tracer is injected into the bloodstream through a vein and then it circulates throughout the body. When the tracer reaches the brain, an amyloid tracer for example, it will bind temporarily to amyloid plaques if there are any. Tau tracers will bind to tau tangles. And glucose will be taken up by metabolically active brain cells. When the tracer sticks to its target, it emits positrons that are detected by the scanner before the tracer washes out. Radioactivity is always a health and safety concern, but the amount of radioactivity from a PET scan is relatively low, similar to what one gets from a chest X-ray.

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Glucose is the major fuel for brain cells. In Alzheimer's disease, frontal lobe dementias, and possibly even Lewy body dementias, there are distinctive patterns of metabolic activity. These scans are approved and usually covered by insurance and can provide useful biomarker information for distinguishing different types of dementia whose symptoms can often look similar.

Amyloid PET scans are especially accurate for identifying the presence or absence of Alzheimer's disease in the brain. Beyond helping with clinical diagnosis, amyloid PET neuroimaging was extremely informative in the recent clinical trials for Alzheimer's disease treatment using anti-amyloid immunotherapy. In these trials, there was a dramatic lowering of amyloid in the brain, as measured by amyloid PET imaging, sometimes down to normal undetectable levels.

Tau PET imaging, while still pretty new and not yet approved for clinical use, may turn out to be even more informative than amyloid PET. The reason for this is that tau PET imaging allows us to see not only if the disease is present in the brain, but how far it has spread through the brain. This ability to stage the disease may be very important in selecting the right treatment for the right patient at the right time.

Spinal fluid tests are also extremely informative in the diagnosis of Alzheimer's disease and other types of dementia. A sample of the spinal fluid, which is safely collected in the lower part of the back in a simple procedure called a lumbar puncture, can be used to measure a host of brain proteins and other chemicals. Spinal fluid analysis provides an enormous amount of information about the health of brain cells. Not only can we measure levels of amyloid and tau, but we can measure many more and varied proteins for inflammation, degeneration of synapses and different types of brain cells, oxidative stress, injury to the blood vessels of the brain, and metabolism. Spinal fluid tests for amyloid and tau are approved for clinical diagnosis and usually are covered by health insurance, and they provide equivalent information or more compared with amyloid PET scans.

The most exciting and important progress in the dementia field over the last few years has been the development of blood tests for Alzheimer's disease. With new, highly sensitive and specific lab reagents and technologies, we can now detect the extremely low levels of tau, amyloid, and some other brain proteins that are produced in Alzheimer's disease and leak out into the bloodstream. While these tests are as yet not as accurate as PET scans or spinal fluid tests, they will be extremely useful for screening purposes and possibly for monitoring response to new treatments. They will help in establishing a positive diagnosis of Alzheimer's disease or other conditions affecting our cognitive abilities as we age. They are also essential in clinical research for new treatments for Alzheimer's disease as they allow us to measure whether a new drug or other treatment is working and give us insights into how the drug might be working—for example, by looking at changes in the levels of amyloid, tau, inflammation, or other features of neurodegeneration with use of the drug.

Biomarkers are an active area of research. As more biomarkers are discovered and as we better understand the information that each biomarker is giving us, how to measure them, and how to use them, the value of biomarkers in understanding, diagnosing, treating, and monitoring Alzheimer's disease will continue to increase.

Steven E. Arnold, MD

Professor of Neurology
Harvard Medical School
Managing Director
Interdisciplinary Brain Center, Massachusetts General Hospital

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