Alzheimer's Disease is a great fear for many individuals, and for the health care system as it may well eclipse heart disease in costs as the “Boomers” age. And it is a global problem. The research into the underlying causes and treatment have been intensifying but have been a bit undisciplined; it is hard to study a disease when it is characterized by a cluster of symptoms, defined medically as a syndrome, rather than a diagnosis based on objective biological evidence. In a whitepaper in The Journal of the Alzheimer’s Association researchers have created a framework to describe Alzheimer’s diagnostically and to begin to recognize its trajectory, what we used to call its natural history.

The framework was developed by the National Institute on Aging, the Alzheimer’s Association, as well as other stakeholders, including patient advocates, Big Pharma and the FDA. Rather than relying on the patient’s symptoms of memory loss, difficulty finding words or confusion the framework identifies objective findings, one based on images of the brain and the other on chemicals in the blood, biomarkers. Because the can be both readily measured and standardized we can now separate the phenotype – what a person seems like, from their biological markers. Three markers are utilized.

- A is for amyloid-proteins that are sticky causing them to clump together in clusters perhaps blocking cell signaling or activating the immune system to destroy the affected cells. The presence of amyloid in spinal fluid, obtained from a spinal tap or identified in PET [1] imaging are diagnostic.
- T is for tau-proteins that are involved with the roadways (microtubules) for the transit of metabolic products and other essential components within cells. They are like guardrails, and as they are destroyed, they collapse into tangles and close those cell highways. Again, their
presence in spinal fluid or identified on PET studies are diagnostic.

- N is for neuronal injury – in Alzheimer’s Disease (and in other degenerative diseases) specific areas of the brain get smaller. This is often a finding but is non-specific it can be a marker for other neurodegenerative diseases.

This simple classification system allows the previous efforts at Alzheimer’s research, a Tower of Babel diagnostically, to speak with one voice. And while this seems to be simple, it took a while to achieve a scientific consensus; it is the nuts and bolts of day-to-day research rather than the sound bit for the evening news. By adopting the framework, the global community can talk about the disease and know we are talking about the same general group.

Another value is that by using three markers, you can begin to break the homogenous group of Alzheimer’s patients into hopefully meaningful subgroups so that you can determine whether therapy is effective for the aggregate (which till now has been frustratingly unsuccessful) or perhaps for some readily identified subgroup. Creating possibly biological subgroups is how we will personalize care.

Finally, this simple nomenclature allows for the possibility of characterizing the spectrum of Alzheimer’s phenotypical presentation, from sub-clinical as we might talk about being pre-diabetic, to early stages where treatment efficacy could be established to later stages when palliative care is more helpful. Specifically, the framework states that amyloid changes in the absence of Tau changes are consistent with “Alzheimer’s pathologic change;” and the presence of both biomarkers would be termed Alzheimer’s Disease. I would hasten to add that these are not separate entities but are stages of a biologic process, the Alzheimer’s continuum.

I bring this work to your attention because it will not be on the evening news, nothing titillating to tease the audience, no way to fashion this as a dramatic breakthrough. But it is how science and particularly clinical medicine works. In 1906 the first description of Alzheimer’s Disease was recorded, 1984 beta-amyloid identified, 1986 tau identified, 2009 the first attempt was made to standardize Alzheimer’s biomarkers. It took another nine years to reach a consensus; science has its own timescale. This is a small success in a much more protracted battle; I just wanted to call your attention to the quiet work scientists and clinicians do.

[1] PET is positron emission tomography. It is a form of imaging where a patient is given radioactive material that can be traced with a gamma camera, a sophisticated form of a Geiger counter. The resulting images provide views, in this case, of the brain, that are not as well defined by MRI or CT scanning.

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