

Amyloid in the Brain, Alzheimer's on the Mind

BY JASON KARLAWISH

In hindsight, Angela Deter thought, perhaps she should've been less forthcoming about joining what she called "the Alzheimer's prevention study."

A minor slip at the office—a struggle to name encryption software—brought a quip from a colleague: "Must be the amyloid at work." (Amyloid is one of two pathological signatures thought to cause Alzheimer's disease.) Laughter followed, and then the forgotten name, and all moved on, but Angela was angry, hurt, and speechless.

Another day at the office. Another day at risk for dementia caused by Alzheimer's disease.

America has embarked on a great biomedical and public health moonshot mission to take on the Alzheimer's problem. Goal number 1 of the United States' national Alzheimer's plan is discovering treatments that prevent and effectively treat the disease by 2025.

"Angela" is an alias, and some details are altered for her privacy, but her story is real. She is one among thousands of brave volunteers enrolled in studies to discover these treatments. At the Penn Memory Center, where I am a physician and codirector, she is part of a five-year test of a drug in cognitively unimpaired persons sixty-five to eighty-five years old with evidence of what my coinvestigators and I describe as "elevated amyloid" in their brain. The study aims to demonstrate that a drug targeting amyloid will slow the cognitive decline in persons whose brain scans show this elevation.

Her colleague's quip shows how sharing this information can affect relationships. He's thinking of Angela differently than he did before she told him of her plans to join the study. Her son urged her to move closer to him "before it's too late." Reactions like these reveal the notable ethical challenges of learning you're at risk of having a disease of grave consequences with uncertain causation.

Men and women, Democrat and Republican, young and old, rich and poor frequently use "silver tsunami"—a disaster metaphor for the aging of our population—to voice fears about an underproductive or underemployed labor force;

lack of money in the face of illness; neglect from a health care system ill equipped to care for the disabled; and smaller, scattered, divorce-sliced-and-diced families struggling to come together to care for one another.

It's no wonder Alzheimer's is on everyone's mind.

Alzheimer's prevention studies promise to turn the disease into a manageable problem. When an effective preventive medication is discovered, I, like my colleagues in oncology, will assess patients for disease progression, adjust drug dosages, order follow-up scans, and so on.

I'm oversimplifying, of course. Twenty percent of patients diagnosed with Alzheimer's disease by experts like me in fact don't have elevated amyloid and so, in fact, don't have Alzheimer's. What they *do* have is the subject of intense research, and there are many possibilities. A recent study of one thousand brain autopsies from older adults with a range of cognitive impairment showed at least 230 combinations of neuropathology. The point is that while the disease will be treatable, we're unlikely to defeat it as we did polio and smallpox. We're going to have to learn how to live with Alzheimer's as an at least somewhat treatable disease.

We need to think outside the biomedical box. People are living and working longer, and so workplace protections and reasonable accommodations will need to be scrutinized. Declines in the ability to drive, errors in financial transactions, and being a victim of fraud or abuse are among the earliest signs of cognitive decline. Imagine a future with a system that monitors Angela's car and her many financial accounts to inform me that she's having problems and needs to come in to see me. Libertarians will swoon over such scenarios.

Our national mission needs more than doctors and scientists. We need poets and creative types to take on the lurid metaphors of silver tsunamis, epidemics, devils, demons, and the living dead that have made Alzheimer's into a gothic horror story.

We need different stories. I don't mean "happy stories." This is a lousy disease, but Angela is looking for words. Imagine she had told her colleague that she may have amyloid on her brain but she still has feelings in her heart and she enjoys her work.

Living with the disease

Jason Karlawish is the codirector of the Penn Memory Center and a professor of medicine, medical ethics and health policy, and neurology at the University of Pennsylvania. DOI: 10.1002/hast.904