

1 PHYSICIAN HEAL THYSELF

An email with a black box warning! That's what I got 11 years ago after Lois and I submitted saliva samples to a DNA testing service. Lois is the family genealogist, and she thought that DNA testing would be helpful in filling in some of the missing branches of our ancestral trees. In addition to lists of DNA relatives, the report included many risk genes for a variety of medical conditions, none of which were present for either of us. However, this locked black box contained two genes of neurological interest. A mutation in the *LRRK-2* gene is the most common cause of hereditary Parkinson's disease, and the *APOE-4* allele is the most significant genetic risk factor for late-onset Alzheimer's disease.

I am a general neurologist, and I knew about these neurological risk genes. About six years before this, I had started to lose my sense of smell. I thought this was most likely due to normal aging, but within five years I could not smell anything. I also had illusory odors, called phantosmias. These were like the smell of baking bread mixed with perfume. At first, these smells occurred several times a week and lasted a few minutes. Over the next few years, they became less frequent and finally disappeared entirely. About 80% of people with Parkinson's disease lose their sense of smell, usually some years before the tremor and gait problems develop. Phantosmias have been reported in people with Parkinson's disease. Given my olfactory symptoms, I wondered if I might be on the path to Parkinson's disease, so I unlocked the black box to see if

I had the *LRRK-2* mutation. I didn't have that. What I did have was two copies of the *APOE-4* allele giving me a 50% chance of having a diagnosis of Alzheimer's dementia by the age of 70 and making it almost certain that I would have it by the age of 80. It turns out that virtually all people with Alzheimer's disease have at least some loss of smell, but most are not aware of it until tested. My loss of smell had been my canary in the coal mine, but I had been unaware of its significance. Before getting my *APOE-4* results, Alzheimer's was just not on my radar screen. Both of my parents had died in midlife from cancer, but looking back a generation or two, there clearly was a family history of dementia.

I was stunned by this news. I was 61 years old and still active, teaching neurology to residents and medical students, and providing care for a variety of patients with neurological problems, including dementia. I traveled to Tanzania every year to teach neurology there as well. Cognitively, I thought I was still doing fine, but I asked a friend who is a dementia specialist to do some cognitive testing on me. Everything was normal, but there were some caveats. In all cognitive domains but one I scored in the 95th percentile. However, in verbal memory, I was in the 50th percentile, still normal, but it was a sign that there might already be some subtle damage to the part of my brain that deals with language.

A year later, when I was 62, I retired. I wanted to make sure that I didn't wait until I made a mistake in the care of my patients. I plunged into the neurological literature to find out what was known about slowing the progression of Alzheimer's disease. I found that there was consistent evidence that regular aerobic exercise can slow progression of the disease by as much as 50%. Plant-based diets such as the Mediterranean diet or a variant called the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet with a greater emphasis on berries and nuts have been

shown to slow progression by 30–50%. Other lifestyle modifications that appear to be beneficial include staying intellectually and socially active, getting at least seven hours of sleep per night, and controlling cardiovascular risk factors such as diabetes, high blood pressure, increased cholesterol, obesity, and smoking. Fortunately, I quit smoking when I was 18, and I follow these other guidelines religiously. I think it is making a difference.

I also want to do everything I can to help move the science about Alzheimer's forward. I have participated in six research studies so far. These include three clinical trials of medications, two technology-based studies, and a longitudinal neuroimaging study using amyloid and tau PET scans to follow the progression of Alzheimer's in my brain. I don't expect that any of these studies will cure me, but I hope that, by my participation, we can come a little bit closer to finding solutions to prevent, slow, or even reverse this disease.

I feel strongly that people with Alzheimer's disease and their families should feel comfortable talking about their journeys with family members, friends, and neighbors, and, if possible, with the general public. Stigma and misconceptions must be addressed. For example, the pathological changes in the brain, the amyloid plaques and tau-containing neurofibrillary tangles, appear very early, as much as 20 years before any cognitive issues arise. These 20 years before cognitive decline begins may well turn out to be the most effective time to stop or at least slow disease progression. Several current studies are looking at the efficacy of treatment in this presymptomatic period. But overcoming the stigma of Alzheimer's can be a barrier to recruiting research subjects who are at risk but who do not yet have cognitive impairment.

Although I was uneasy at first, I have come to enjoy talking to people about Alzheimer's disease. I have written a book about my experiences for the general public titled

A Tattoo on my Brain: A Neurologist's Personal Battle against Alzheimer's Disease, and I have given over 35 interviews and talks for radio, television, podcasts, newspapers, magazines, medical students, book groups, and Alzheimer support groups.

My Alzheimer's disease is slowly progressing. My most recent cognitive tests put me at the border between MCI and early Alzheimer's dementia. There is more amyloid and tau on my recent PET scans. But I am adapting to changes with the support of my wife, family, and friends. Life is still good, and I expect it to continue being good for many years to come.

Note: This essay is based on an article with a similar title published in Alzheimer's TODAY: The Official Magazine of the Alzheimer's Foundation of America, 2023; Volume 18, Number 1, pp. 18–19; a quarterly publication of the Alzheimer's Foundation of America https://alzfdn.org/wp-content/uploads/2023/03/ALZ-TODAY-18.1_MECH-HR.pdf.