

# INTRODUCTION

I am a retired neurologist with early-stage Alzheimer's disease. Although I cared for many patients with Alzheimer's disease and other dementias during my career, it never occurred to me that I might one day have it too. I do. So now I'm on the patient's side of the experience, an expert from the inside out on my own early-stage Alzheimer's as it stakes out its slowly growing presence in my brain

The operative phrase here is "slowly growing." Most Alzheimer's patients are diagnosed when symptoms of the disease show up in their behavior or cognitive functioning – they may seem noticeably "off" to those who know them or to themselves. That's typically around the time that the damage to brain cells has become moderate to severe. I found mine much earlier because I went looking for it. It was a fluke, really, that I stumbled across some genetic information that prompted my clinical search. It's easy to say I'm unlucky to have Alzheimer's. But in truth, I'm lucky to have found what I found when I found it. That has meant all the difference, as it has enabled me to access cutting-edge medicine through clinical trials and other progressive treatment options. And I've made some simple lifestyle choices about diet, exercise and social and intellectual activity that evidence-based science has found beneficial for brain health and resilience, including for those with Alzheimer's. Along the way, I've also discovered that nature itself is an impartial guide on this journey. Whether it is in cells viewed through the most sophisticated technology, the earth underfoot on a walk,

or the currents that shape a day on the river, the lessons emerge. As a scientist and physician, I want to share this lifeline with others.

It might seem that *early-stage* Alzheimer's disease, with imperceptible or only mild cognitive impairment, has little to teach anyone outside a highly specialized subset of neurologists and research scientists who work with it. I suggest otherwise. In the most universal sense, a diagnosis of Alzheimer's disease is clarifying; it presents the uninvited opportunity to confront your own mortality and get serious about making the most of the time you have. In concrete terms, the sooner you know a disease process has begun, the sooner you can take reasonable steps to stop or slow that process and review your other life priorities. What's really important to accomplish in the time you have left, perhaps checking that bucket list and strengthening connections to friends and relatives. At a societal level, science and statistics show a perfect storm already under way and growing around Alzheimer's: incidence of the disease escalating, a shortage of medical and care specialists, an overwhelming burden on primary care physicians who are underprepared and inadequately trained to provide effective care, and an unimaginable struggle for families and patients themselves. This is no small subset of Americans. Some 5.8 million American are living with Alzheimer's dementia today, a figure projected to reach 14 million by 2050. The worldwide prevalence of Alzheimer's disease and related dementias was estimated to be 35 million in 2010 and expected to rise to 115 million by 2050 [1]. Most dementia patients in high-income countries are diagnosed at the moderate to advanced stage, when noticeable symptoms first prompt medical attention. In limited-resource settings, many people never receive care for dementia or arrive at a hospital or clinic only in the end-stages of their disease.

Dementia is a degenerative disorder of the brain that causes loss of memory and disturbances in thought processing

in excess of those of normal aging. These changes in the brain impair a person's ability to perform everyday tasks and activities, and affect their ability to communicate with others – listen and respond – and maintain their part in relationships. Alzheimer's disease accounts for at least 60 percent of cases of dementia, although other causes, including Parkinson's disease, can sometimes be difficult to distinguish from Alzheimer's by symptoms alone and sometimes occur in combination with Alzheimer's in the same person.

A definitive diagnosis of Alzheimer's disease requires evidence of the amyloid plaques (clumps of protein fragments) and neurofibrillary tangles (twisted fibers formed from another kind of protein) in the brain that were discovered by Dr. Alois Alzheimer in 1906. Until relatively recently, this evidence could only be obtained by examining the brain microscopically after death. Now there are biomarker tests that can provide good information about the presence of Alzheimer's pathology during life. These include spinal fluid tests for the amyloid protein found in the plaques and the abnormal tau protein found in neurofibrillary tangles. PET scans of the brain can now show the location of these proteins, and blood tests for both amyloid and tau may be available soon.

Research using these biomarkers has shown that the first abnormality in the brain of a person with Alzheimer's, the formation of plaques, starts to occur up to twenty years before there are any cognitive symptoms – signs of dementia. The tangles and subsequent death of nerve cells that result in brain atrophy start about the time of the first symptoms of cognitive impairment or even a few years before. This realization that abnormalities in the Alzheimer's brain start years before any symptoms occur has led to the idea that effective, disease-modifying treatment would ideally be started in the earliest stages of the disease, perhaps well before there are any symptoms.

Traditionally, Alzheimer's disease has been synonymous with Alzheimer's dementia. A diagnosis of Alzheimer's disease depended on symptoms of dementia being present. Some experts in the field still hold to this strict definition. That's begun to change, however, in the past two decades, since we've learned conclusively that the pathological changes in the brain start ten to twenty years before there is any cognitive impairment. Many experts now hold that we should include in our definition of the disease these pre-symptomatic years when the brain changes are occurring but cognition is still normal, so that interventions to slow that disease process could start sooner. I am one of them.

While experts in my field continue to debate how to define early-stage Alzheimer's in diagnostic terms, we have tests that can spot the disease process under way, affording precious time for those like me, who could be taking steps that evidence-based science suggests can slow the cognitive decline of Alzheimer's disease. I only wish these tests had been available through the many years when the first I saw of Alzheimer's patients was when they were referred to me with cognitive impairment already well advanced.

I have retired from practice, but that just means I've had more time to devote to raising awareness about early-stage Alzheimer's and what we can do about it.

In the fall of 2018, three years after my diagnosis and five years after my retirement, one of my neurologists at the UCSF Memory and Aging Center encouraged me to write a paper directed to neurologists about my experiences as a patient with Alzheimer's disease. In that paper, published in *JAMA Neurology* in spring of 2019, I strongly advocated for early awareness and diagnosis of Alzheimer's [2]. The reasons have only become more compelling with the passage of time:

- New studies continue to advance the scientific understanding of the genetic and other biological

and environmental factors that converge to cause Alzheimer's and other forms of dementia. They show a more nuanced view of the disease progression. At the same time, other new studies underscore the protective benefits that diet, physical and mental exercise, social activity, and potentially some medications provide against neurodegenerative decline, including Alzheimer's.

- Innovative genetic technologies are swiftly transforming possibilities, at times so swiftly that they challenge the more deliberate and cautious presentation of medical information customary in generations past. Ancestry trackers like 23&Me and Ancestry.com provide individualized genetic data for customers who want to see theirs. This easy access for consumers can be helpful. But the methods any company uses to harvest the data, the quality of it and how individuals will interpret it and act on it – often without ever consulting their doctor or a genetic counselor – leaves users vulnerable.
- The number of clinical trials for drugs and other therapeutics searching for a way to slow the progress of neurodegenerative disease has increased dramatically, meaning that there are more opportunities for individuals to participate, and more opportunity for doctors to flag relevant clinical trials for a patient's consideration.

We continue to see mounting evidence for gains possible in identifying Alzheimer's at the earliest stages, to slow or even stop cell damage, years before symptoms might predictably emerge. The hope for the future is unfolding on multiple fronts, with progress emerging every day in the urgent quest to bring the best in medical science from bench to bedside.

Meanwhile, media coverage of Alzheimer's and related research are often highly technical, frequently conflicting, and sometimes over-simplified and misleading, creating more confusion than clarity about Alzheimer's disease and what can be done about it. Well before the coronavirus crisis struck, the steady stream of Alzheimer's news had led to a kind of update fatigue for many, especially those keen to see new research findings deliver quick results bedside. All the more so today, slowing the progression of the disease and the move by so many to nursing care facilities are imperative. My hope with this book is to help readers see the mosaic of findings in a more practical and helpful picture. While no single study has cracked the code for an immediate cure, each one contributes to our understanding in ways that eventually will lead to more effective treatment and prevention. In the meantime, we are not helpless, but the fear and stigma of Alzheimer's can make us feel that we are.

Despite the advances that support earlier diagnosis and treatment of Alzheimer's, assumptions of helplessness and despair have dominated the public conversation. The same is often true in the medical community. Urged by colleagues, I began writing this book as an expansion of that *JAMA Neurology* paper published in 2019, to press for change in the medical profession, especially among those physicians on the front lines with patients who might benefit. But there's no reason that, as individuals, we have to wait for institutional change. We can take reasonable, responsible evidence-based steps to help ourselves.

There is so much at stake in any one person's life. Years of cherished shared time with loved ones, as I have enjoyed with my wife, children and grandchildren. Years to enjoy our favorite things, and friends, colleagues and others in so many ways. All of us – those with Alzheimer's or at high risk of it, families, friends and caregivers, researchers and

research funders, the healthcare industry and public policy makers – we all stand to gain.

Alzheimer's at any stage is a tough disease, in part because, at any age or stage, just knowing that you're living with it is enough to upend assumptions you may have had about the future. It calls for conversations that may be tough, too, whether that conversation is with your doctor, family, friends or others. Among my patients and others I've known who've received a difficult diagnosis, some choose to bare their innermost feelings, others don't. Everyone has their own coping style. I respect them all. As for me, as odd as it might seem, I'm fascinated by this disease that, for my entire career as a scientist and a neurologist, I could only observe from the outside. Now I've got a front-row seat – or, rather, I'm in the ring with the tiger. Of course I'm disappointed that I have Alzheimer's. But I'm stuck with it. And the habits of a lifetime – to approach a question with a certain kind of detachment and to study, experiment, hypothesize and discover – turn out to be my coping mechanisms. I'm grateful for that now. I hope that this book, informed by that perspective on the science, medicine and everyday life experience of early-stage Alzheimer's, will be of help to others.

Following publication of my essay in *JAMA Neurology*, KATU-TV in Portland featured me in a story about the importance of early diagnosis. I was surprised by the number of people who saw it and commented (<https://katu.com/news/local/retired-neurologist-with-alzheimers-shares-importance-of-early-awareness>).

Just like that, my diagnosis went from private to public, and my wife Lois and I heard from lots of people – neighbors who hadn't known, or total strangers, many with sad condolences or sympathy. It could be awkward, honestly, since I was for all practical purposes fine – able and active – while many of them had far more difficult things going on in their lives. That is especially true today, as the Covid-19

pandemic has forced us all to confront our mortality, to grieve losses and, for many, to live in dread of an uncertain future.

What we realized in early 2019 was that the conversation about Alzheimer's had long been stuck on fast-forward to the late stage, end-stage loss, the fear and stigma of the disease, not recognizing the years – even decades – of meaningful time that can be maximized with early diagnosis and treatment. I set out to write this book to normalize that conversation so that more people can learn about those possibilities in time to make a difference. I realize now that some of the lessons I've learned along the way speak to the fears and dread, as well as the hopes and gifts of life in the moment we have, whatever we face.

Most narratives about Alzheimer's understandably focus on the emotional impact of the loss or struggle as the disease advances. My purpose is different: to illuminate the potential of a biologically unique and irreplaceable period of time in which we have the opportunity to change the course of Alzheimer's in any one person's life. This is not false hope or Pollyanna thinking. This is evidence-based medical science, partnered with established findings of the benefits that exercise, diet, social activity and cognitive challenge have been shown to have in regard to the progression of Alzheimer's disease. I share my story not as clinical proof, but simply as medical parable and a call to action for anyone who might be open to encouragement. In the context of the times, I hope this message of optimism adds a sense of agency when we may otherwise feel helpless against the disease.

My experience as someone living with early-stage Alzheimer's gives me the insider's vantage point – one that no one would welcome but which I accept and engage in as an opportunity to continue my life's work. My motivation is two-fold: Personally, I want to live fully and savor the time I have with those I love, doing the things I love.



Professionally, as a physician, and earlier as a research scientist, my purpose has always been to help others. This book embodies my determination to continue to work in whatever capacity I can, to do as much as I can for as long as I can, to benefit as many as possible.

The challenge and pleasure of writing this book – living this book – are all the more intensely felt in some ways as holding my own against Alzheimer’s and making the most of the time I have. Against any chronic degenerative disease, clinicians measure the success of treatment by its contribution to “a meaningful outcome.” For any of us, I believe, that is the universally desired outcome: a life with meaning. That is the story of *A Tattoo on My Brain*.

## Chapter-references

- 1 Prince M, Bryce R, Albanese E, *et al*. The global prevalence of dementia: a systemic review and meta-analysis. *Alzheimer’s & Dementia* 2013; 9:63–75; <https://doi.org/10.1016/j.jalz.2012.11.007>.
- 2 Gibbs, DM. Early awareness of Alzheimer disease: a neurologist’s personal perspective. *JAMA Neurology* 2019; 76:249; <https://doi.org/10.1001/jamaneurol.2018.4910>.