Alzheimer’s dementia or Alzheimer’s disease – What’s the difference and why should we care?

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I now have a special interest in Alzheimer’s disease. For nearly twenty-five years, I practiced general neurology in Portland, Oregon. Some of my patients had dementia, a progressive neurological disorder that causes severe cognitive impairment affecting memory, language, motivation and mood, interfering with everyday activities. There are several neurodegenerative diseases that can cause dementia including Lewy-body disease, Parkinson’s disease, frontotemporal degeneration, and vascular dementia, but Alzheimer’s disease is the most common cause, accounting for 60 – 80% of cases. In 2013 I retired because I had developed mild cognitive impairment (MCI) that was soon shown by biomarker testing to be due to early-stage Alzheimer’s disease. I suddenly wore two hats – that of a retired physician with a lot of experience treating Alzheimer’s disease and now a person living with the same disorder (Gibbs, 2019).

There has been a lot of confusion and disagreement about the difference, if any, between Alzheimer’s dementia and Alzheimer’s disease. Until fairly recently, the terms were often used interchangeably. They both referred to dementia that was confirmed by autopsy to be associated with beta-amyloid plaques and tau-containing neurofibrillary tangles, the neuropathological hallmarks first described by Dr. Alois Alzheimer in 1906. When I was beginning to practice neurology in 1989, we referred to suspected Alzheimer’s as senile dementia of the Alzheimer’s type (SDAT). At that time there was no practical way to make a firm diagnosis during life so we based our diagnosis on our experience with similar patients. Now there are good amyloid and tau biomarkers that have greatly increased the accuracy of diagnosis during life. These include brain PET scans, spinal fluid tests, and most recently several very sensitive and specific blood tests that should be commercially available soon.

Let’s get back to the question, what is the difference between Alzheimer’s dementia and Alzheimer’s disease, and why is the distinction important? Alzheimer’s disease is a continuum. At one extreme is dementia: cognitive impairment that interferes with doing everyday activities, getting more severe over time, and eventually causing death. The dementia phase of Alzheimer’s lasts an average of eight to ten years.

The first symptoms of cognitive problems usually don’t interfere with daily activities. Work may still be possible. This phase is called mild cognitive impairment (MCI). Like dementia, MCI can be caused by other disorders, but in the presence of amyloid or tau biomarkers, Alzheimer’s is almost always the cause. Dementia and MCI used to be all we cared about. But it is important to understand that Alzheimer’s pathology in the brain, the amyloid plaques and neurofibrillary tangles, begin appearing up to twenty years before the first symptoms of cognitive impairment. There is disagreement about when we should start calling this spectrum Alzheimer’s disease. Those who would restrict the term to people with dementia or MCI argue that many people who have positive amyloid or tau biomarkers in middle age will never develop dementia. They might die of something else first, or they might have a resilient brain that resists these pathological changes. Why should we alarm these people who may never get Alzheimer’s dementia? I understand this point of view. However, I think we should be receptive to the idea that the early, pre-symptomatic stage of Alzheimer’s disease is likely to be the most effective time to attack the disease, to slow or even stop progression before any symptoms have occurred. We can already slow progression with evidence-based lifestyle modifications in midlife: getting adequate aerobic exercise, eating a Mediterranean-style diet, staying intellectually and socially engaged, getting adequate sleep, and managing cardiovascular risk factors such as hypertension, hyperlipidemia, diabetes, and smoking. New medications to treat Alzheimer’s disease, like the controversial FDA-approved aducanumab and similar anti-amyloid monoclonal antibodies, may turn out to be more effective if used early, during MCI or even before cognitive symptoms are present. This is not a new idea. Although the anti-amyloid monoclonal antibody solanezumab failed to slow cognitive impairment in subjects with mild dementia due to Alzheimer’s disease, (Honig et al., 2018) a long term, placebo-controlled study of solanezumab in older, cognitively normal subjects with positive amyloid PET scans has been underway since 2014 and will finish at the end of 2022 (Clinical trial, 2022). Two newer anti-amyloid monoclonal antibodies that are more effective in removing beta-amyloid, donanemab (A donanemab, 2022) and gantenerumab, (A
study to evaluate, 2022) are undergoing trials in subjects who do not yet have any cognitive impairment but have positive Alzheimer’s biomarkers. They don’t have Alzheimer’s dementia yet. They don’t even have MCI. But they are on the Alzheimer’s continuum and are at high risk for developing dementia in the future. Very recently, the anti-amyloid monoclonal antibody lecanemab was reported in a phase 3 trial to reduce clinical decline in subjects with either MCI or mild Alzheimer’s dementia by 27% after 18 months. These encouraging results have so far appeared only in a press release, (Lecanumab confirmatory phase, 2022) but if confirmed in a peer-reviewed journal, I would expect a trial in pre-symptomatic Alzheimer’s disease to follow.

So, what’s the difference? Alzheimer’s dementia is the tip of the Alzheimer’s disease iceberg. According to the 2022 Alzheimer’s Disease Facts and Figures, (Alzheimer’s Disease, 2022) there are an estimated 6.5 million people over age 65 with Alzheimer’s dementia now in the US. That seems like a lot. But now let’s add in the number with MCI and positive biomarkers for Alzheimer’s such as a positive amyloid PET scan. That group is estimated to contain more than 5 million people. These are people who are very likely to have Alzheimer’s dementia within a few years. The prevalence of symptomatic Alzheimer’s disease (dementia and MCI) is therefore about 11 million in the US. Now let’s add in the number of people with positive Alzheimer’s biomarkers but no symptoms of cognitive impairment. That group was estimated to be 46 million in 2017 (Brookmeyer et al., 2019). Now we have an estimate of nearly 58 million Americans who have Alzheimer’s pathology in their brains. And most of them are young enough that intervention might successfully prevent dementia.

When should these pre-symptomatic people be identified and offered treatment? Certainly life-style modifications should begin as early as possible, especially in those with a family history of Alzheimer’s disease. For pharmaceutical interventions, we must follow the science as it unfolds. I would predict that our first successes will occur in research subjects who have a family history of Alzheimer’s and who are within a few years of expected onset of cognitive impairment as identified by presence of amyloid and tau biomarkers. Waiting to treat Alzheimer’s until dementia has set in is not likely to be successful. The horses will be already out of the barn.

Conflicts of interest

I have no conflicts of interest.

Data Availability

No data was used for the research described in the article.

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