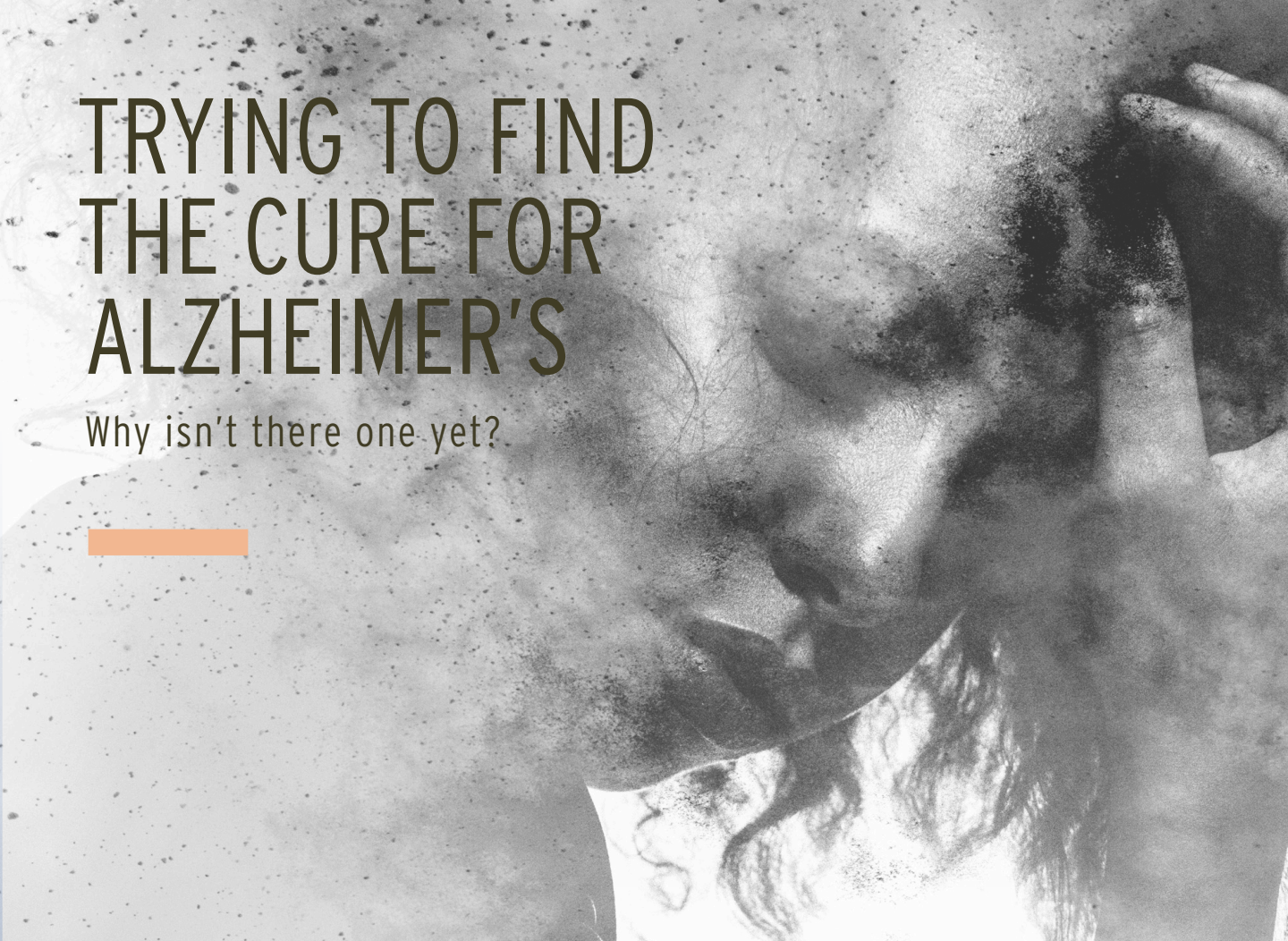
TRYING TO FIND THE CURE FOR ALZHEIMER'S

Why isn't there one yet?



There is growing evidence that it takes a decade or two for Alzheimer's disease (AD) to reveal itself - changes begin in the brain long before symptoms are evident. Historically, that meant that the disease was not diagnosed until late in the process, after symptoms became too noticeable to ignore or brush off as normal age-related cognitive decline.

Researchers focused on trying to treat mid-to late-stages of the disease because those were stages that could be identified, and there was urgent demand for an effective treatment given the devastating effects of the disease.

Several medication trials have failed to improve memory and other thinking skills in people with middle-to late-stage Alzheimer's disease, perhaps because the study participants' brains were already significantly and irreversibly damaged. Researchers thus began trying to intervene earlier in the disease process to see if Alzheimer's disease could be prevented or delayed.

There are clinical drug trials underway now with individuals who have either mild cognitive impairment (MCI) or early Alzheimer's disease and "these are important efforts," according to Dr. Reisa Sperling of Boston's Brigham and Women's Hospital and Harvard Medical School .

Dr. Sperling believes that, similar to cardiac disease and cancer treatment,

ALZHEIMER'S DISEASE IS PROBABLY OPTIMALLY TREATED BEFORE COGNITIVE IMPAIRMENT IS EVIDENT,

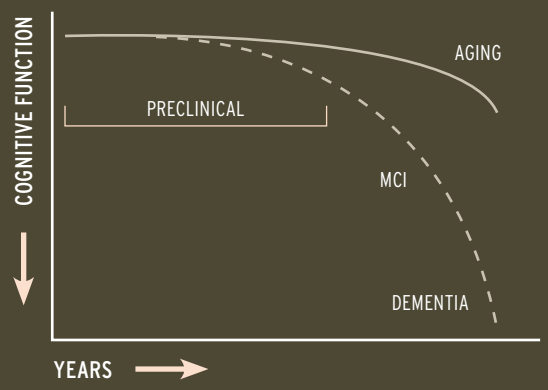
during what is referred to as the preclinical, or presymptomatic, stage. "While it's important to study all stages of the continuum of Alzheimer's disease," explained Dr. Sperling, "I am particularly excited that there has been a recent shift to conducting trials with people during the preclinical stage that precedes MCI."

Advances in brain imaging and genetics have allowed the expansion of research to include these prevention trials that target cognitively normal, but at-risk individuals.

A4 STUDY

Dr. Sperling is the Project Director for one of these innovative prevention trials, the A4 Study. This trial targets cognitively-normal people aged 65 to 85 years that have been screened for the presence of early amyloid-beta plaque (Aβ) build up in their brains. The presence of Aβ is a known hallmark of Alzheimer's disease so this trial is seeking a way to reduce or halt Aβ >>

THE CONTINUUM OF ALZHEIMER'S DISEASE



Alzheimer's disease (AD) progresses through a long continuum that looks like normal aging during the earliest part, as shown in the above image. During the preclinical stage, gradual changes are occurring in the brain but the individual is not yet experiencing any noticeable symptoms. MCI (mild cognitive impairment) comes next, followed by dementia, which itself is often classified in three sub-stages (early, middle and late). It is important to note that not everyone who experiences early changes in their brain structure goes on to develop MCI, and not everyone with MCI goes on to develop AD.

Source: "Toward defining the preclinical stages of Alzheimer's disease" in Alzheimer's & Dementia, May 2011

accumulation, hoping that will prevent cognitive decline.

A cure would be the ultimate discovery, but even if one isn't found, a treatment that delays onset would be monumental. Dr. Sperling explained that

"IF WE FOUND AN INTERVENTION THAT DELAYED THE ONSET OF ALZHEIMER'S BY FIVE YEARS, THAT WOULD RESULT IN A 57 PERCENT REDUCTION IN THE NUMBER OF PATIENTS WITH THE DISEASE."

Half of the participants in the A4 study receive a monthly IV infusion of the drug solanezumab for 3.25 years while the other half, the control group, receive a placebo (a harmless substance containing no medication). During the trial, participants will complete a variety of tests including ones that monitor any changes in their cognitive functioning.

The first participant began IV infusions two years ago, however the project won't conclude until 3.25 years after the last participant begins. Enrollment in the trial will continue until they reach 1,150 participants. The study is being conducted at 67 sites, 65 of which are in Canada and the US, plus one in Australia and one in Japan. To learn more about this study or to participate, visit: *http://a4study.org/.*

GENERATIONS TRIAL

Another example of a prevention trial now underway is the Generations trial. This one targets people who are at high genetic risk for developing Alzheimer's disease based on testing for the AD risk gene APOE4. Butler Hospital in Providence, Rhode Island is one of the sites for this clinical trial, and Dr. Stephen Salloway heads the research team there. (Butler Hospital is one of the sites for the A4 trial as well.) Dr. Salloway explained, "The Generations trial will test two medications, an anti-amyloid vaccine and a beta secretase inhibitor, for their ability to delay the onset of memory loss."

Individuals with normal memory function, aged 55-75 years, can sign up at www.endalznow.org/genematch and receive a kit to perform a cheek swab at home and mail it back to test for the APOE gene. The researchers are looking for people with two copies of the APOE4 gene since that indicates a very high risk of developing Alzheimer's disease. It will be a particularly challenging task to identify suitable participants for this trial because as Dr. Salloway noted, "only approximately 2-3 percent of the population has two copies of the APOE4 gene." The researchers will therefore need to screen 100,000 people to find those at highest risk for the study.

GETTING INDIVIDUALS TO TAKE ACTION EARLY

In this publication the article "Millennials Have The Power To Prevent Their Own Cognitive Decline" on (page 14) WBHI emphasizes the importance of making lifestyle changes early to keep your brain healthy and try to prevent dementia, and in the article "The Need to Know Sooner" (page 21) WBHI discusses the widespread consensus about the importance of early diagnosis. Making healthy lifestyle choices to support your brain health and seeing your doctor immediately if you have any concerns about your cognitive functioning are both important ways that you can take action early to address

Alzheimer's risk. Yet another step you could take, to possibly help yourself and definitely help future generations, is to participate in a clinical trial. "Most participants in our studies decide to participate because they want to protect their children and grandchildren from having Alzheimer's disease," shared Dr. Salloway.

FINDING COGNITIVELY NORMAL, BUT AT-RISK PEOPLE TO PARTICIPATE IN CLINICAL TRIALS IS CHALLENGING AND YET IT IS CRITICAL FOR FINDING A CURE OR TREATMENT.

As Dr. Sperling described, "These people are out happily living their lives. They are not going to their doctor because they have no symptoms, so we have to reach out to these people in other ways." Articles like this one, TV interviews, social media and word of mouth can help raise awareness. "The good news is, once we reach people and raise awareness, we find there is a tremendous amount of interest in participating," said Dr. Sperling.

The two studies described above are only examples and there are many other trials that need participants. The Brain Health Registry (www.brainhealthregistry.org) is a website, led by researchers at the University of California San Francisco that is streamlining the process for getting involved with clinical trials while also helping researchers analyze the brain function of thousands of volunteers over time.

After a simple sign-up process, volunteers provide a brief personal history and take online brain tests (which feel like online games). A select number of volunteers will be asked to do more, e.g., provide saliva or blood tests, or participate in clinical trials. Volunteers may choose to participate as little or as much as they like.

"ALZHEIMER'S DISEASE IS ONE OF THE TOP THREE PUBLIC HEALTH PROBLEMS THAT THREATEN THE STABILITY OF HEALTH CARE ECONOMIES AROUND THE WORLD,"

emphasized Dr. Salloway. "So it's no surprise that the US Congress and G-7 have made finding breakthrough treatments for Alzheimer's disease by 2025 a major priority." Alzheimer's is a devastating illness - for countries, communities, families and individuals. "There's nothing worse than the idea that the body is still healthy but the mind is slowly being lost over a decade or more," expressed Dr. Sperling. "We now have to take the fact that this is a long, slow disease and turn that to our advantage, targeting the earliest stage possible to try and prevent it. And I absolutely do believe that Alzheimer's disease is preventable."