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HEALTH | YOUR HEALTH

Her Alzheimer's Research Includes Her Husband

What life is like for a Harvard professor who helped design the A4 drug trial and is married to one of the study subjects



Dorene Rentz and her husband, Ray Berggren, at their home in Natick, Mass. Dr. Rentz helped design the cognitive tests used in the A4 Alzheimer's clinical trial her husband is now participating in.

PHOTO: M. SCOTT BRAUER FOR THE WALL STREET JOURNAL



By

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Sept. 23, 2019 10:26 am ET

Natick, Mass.

As a lifelong Alzheimer's researcher, Dorene Rentz sees many brain scans with amyloid plaques, a telltale sign of the disease that ravages the brains and memories of its victims.

But there's one scan she's unable to see: that of her husband, Ray Berggren.

Never did she think that one day her 73-year-old husband would be part of a clinical trial she helped design, whose overall cognitive outcomes she will

eventually help analyze.

"I've never been able to look at any of his data, nor do I want to," says Dr. Rentz, a 68-year-old neurology professor at Harvard Medical School. "I don't even know if he's on the drug or not."

Dr. Rentz is one of the researchers involved with the massive A4 (Anti-Amyloid Treatment in Asymptomatic Alzheimer's) study. A4 is testing whether a drug called solanezumab can slow memory loss in people with elevated levels of amyloid plaque in their brains. They may experience no memory loss yet, or report signs of cognitive decline but pass cognitive tests.

Amyloid is a protein produced in the brain that can build up and form plaque deposits that researchers believe play a key role in the development of Alzheimer's disease.

Eli Lilly & Co. makes solanezumab, which failed in previous trials in patients already diagnosed with symptomatic Alzheimer's disease. But researchers hope that by intervening earlier and at a higher dose, they may have success this time.

The randomized controlled trial spans 4.5 years, during which participants get infusions of either solanezumab or a placebo. There are 1,169 participants, all of them 65 to 85 years old.

Mr. Berggren is one of them.



Mr. Berggren goes to Boston University every month to receive an infusion. Neither he nor Dr. Rentz knows if it's a placebo or the anti-amyloid drug, solanezumab. PHOTO: M. SCOTT BRAUER FOR THE WALL STREET JOURNAL

Every month for the past three years he's driven to Boston University for treatment. The study is a double-blind, randomized control trial, so neither participants nor researchers know if patients receive the drug or a placebo.

Every three months he also does cognitive testing to assess his memory, executive function and speed of processing, among other things.

So far, so good, Mr. Berggren says. The retired auditor and database administrator with a sardonic sense of humor rattles off names and dates like a computer. He talks fondly about the seniors he helps with basic iPad and computer questions twice a week at the local senior center.

He handles grocery shopping and cooking at home and manages to function independently—with the company of their cats, Rusty and Lady—when Dr. Rentz travels for work.

But red flags more than a year earlier first caused Dr. Rentz to suspect something may be wrong with his memory.

Dr. Rentz has studied Alzheimer's disease for more than 30 years. The couple experienced the disease firsthand when Mr. Berggren's mother began experiencing memory problems and moved in with them for several years before dying in 2003. "When my husband started to exhibit memory problems, I was like every other caregiver, with my head in the sand," Dr. Rentz says.

The defining moment was when his son gave them a new camera for Christmas four years ago. They took it on vacation. A couple of months later his son called up asking if he could borrow the camera.

"Ray was adamant that he never gave us a camera for Christmas," Dr. Rentz says. "He had no recollection of the camera. And they kept arguing about it and finally I went upstairs and got the camera."

Getting him into the trial wasn't easy. It required some back and forth with Lilly to ensure there was no conflict of interest. (The company declined to comment.) It took four months to make it happen. Mr. Berggren was assigned to Boston University researchers to avoid those conflicts.

"I can't work in this field for 30 years to help find a cure for Alzheimer's disease and then not be able to help the person I love," she says.

Reisa Sperling, a neurology professor at Harvard Medical School, is the principal investigator of the A4 trial, which includes patients at 67 sites across four countries.

Dr. Sperling has worked closely with Dr. Rentz for decades and knows Mr. Berggren well. She says it was important that he not be a participant at their site. "We have to be careful that we in no way influence what his participation in the trial is," Dr. Sperling says.

Her grandfather and father died of Alzheimer's disease. "It's a useful thing for me to always remember the humans on the other side of this important scientific study," Dr. Sperling says. "I have definitely seen this up close and personal and having Dr. Rentz's husband, knowing him as a person, makes me again realize how important the stakes are."

Dr. Sperling says researchers made two changes to the trial in early 2018, after it started, because of the drug's failures in previous trials. They quadrupled the dose given to those receiving the drug and extended the trial to 4½ years.

SHARE YOUR THOUGHTS

Do you have a relative with Alzheimer's disease? When did you first notice their memory slipping? Join the conversation below.

The first patients enrolled in the trial in 2014 began moving to the open-label phase, in which patients in both groups are given the option of taking the drug, in early 2019. They can continue taking the drug until the trial is complete, which is expected in late 2022. (The trial had rolling admission but is not accepting new patients now.)

Lilly and the federal National Institute on Aging are funding the study.

Dr. Sperling says some participants came into the study because of subjective complaints of cognitive decline. To qualify, they had to perform normally on cognitive tests. Then they underwent PET scans to detect amyloid. Those with positive amyloid scans are more likely to have said they noticed subtle cognitive changes and perform a bit worse on memory tests, though they still pass them, Dr. Sperling says.

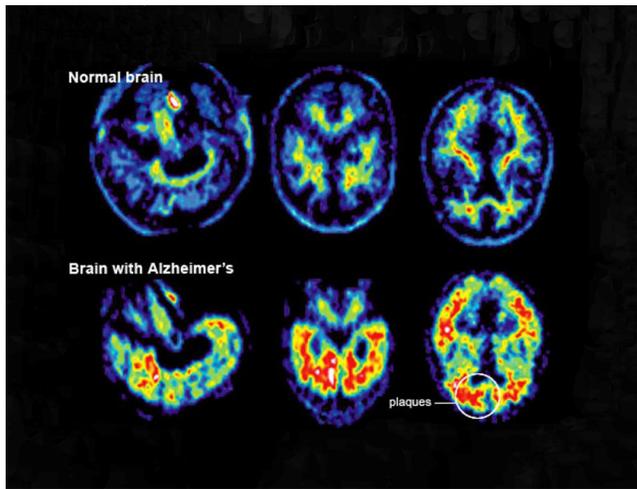
“The amyloid hypothesis has come under quite a bit of fire,” she says. “But this suggests that at this stage of the disease, there is a relationship between amyloid and very subtle memory changes.”

Dr. Rentz met Mr. Berggren in 1992 at a mutual friend's Christmas party. Mr. Berggren, who had two children from a previous marriage, recalls meeting Dr. Rentz. When she introduced herself she spelled her last name.

The next day he looked her up in the phone book. “One thing led to another and we got married four years later,” he says.

They cherish the house they live in, a modified Cape Cod with a spacious backyard. Along with volunteering at the local senior community center, he audits classes at Boston University. Right now he is taking a cybercrime class. Last semester he took a film and literature class. “I'm doing Sudoku all the time on my phone,” he says.

Dr. Rentz worried that her husband's memory impairments might disqualify him from being eligible for the study, but he passed the cognitive tests. The toughest part was when they got the PET scan results showing he was amyloid positive.



Participants in the A4 trial passed cognitive tests. But brain scans show that they have elevated levels of amyloid plaque, a hallmark of Alzheimer's disease, in their brains. PHOTO: SCIENCE SOURCE

“The bad news is you have a positive amyloid scan. The good news is that you qualify for the study,” she recalls thinking.

Mr. Berggren and Dr. Rentz both say he appears to be doing pretty well. When she says he recently repaired the lawn mower, he corrects her. It was the snowblower.

Still, she says, “He forgets events and things. He’ll say, ‘We’ve never done that,’ and I know we have. He’s also forgotten about some of his appointments recently.”

“What husband doesn’t screw up his appointments?” Mr. Berggren exclaims. He says he’s not sure if his memory has gotten worse, but he isn’t fretting over it.

“He’s never been a worrier in that regard,” Dr. Rentz says. “I think a little bit of unawareness is great. I’m not worried either. Yet.”

For now, life goes on. They’ve developed consistent routines to make things easier. She takes the same train every day to work and back. They look at the calendar on Sundays to remind themselves of what’s coming up for the week.

They have plans to go to Chicago for Thanksgiving and on a cruise in January.

“We make the best of what we have today,” Dr. Rentz says. “Ray has always had a great sense of humor and we take life lightly.”

“There’s so many different things that could wrong,” Mr. Berggren says. “Alzheimer’s is competing. I’m just going to try to enjoy life with my wife.”

The Stakes of the A4 Trial

Amyloid plaques, one of the hallmarks of Alzheimer's disease, can appear in the brain 10 to 15 years before someone receives an Alzheimer's diagnosis.

Together, amyloid and tau—another protein that forms tangles inside nerve cells—disrupt neural networks and are believed to lead to memory impairment and eventually symptoms of Alzheimer's disease.

Having amyloid plaques doesn't guarantee that you will later develop clinical Alzheimer's disease, though it's considered a good predictor. The theory, says Ronald Petersen, director of the Mayo Clinic Alzheimer's Disease Research Center in Rochester, Minn., is that at a certain point of amyloid accumulation, the tau accelerates, resulting in the onset of Alzheimer's disease symptoms.

Researchers are closely watching the A4 trial, given the failures of previous anti-amyloid drugs.

"I'd like to see some clinical signal that would motivate me to be more enthusiastic about moving earlier with some of these" drugs, Dr. Petersen says. "But it hasn't happened yet. I think the A4 trial is positioned to really answer some of these questions....If the A4 trial is negative, that will be a serious problem for the whole amyloid treatment approach."

He believes research needs to continue on all fronts, be it targeting amyloid and tau or looking at some of the proteins that define other neurodegenerative diseases, like Lewy body dementia, and vascular disease.

"There's not going to be a silver bullet that is going to stamp out this disease," Dr. Petersen says. "It's going to take combination therapy."

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