Search for Alzheimer’s drug flounders

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Daniel Bradbury with his partner, Jordan Evans, and their twins Jasper and Lola. Mr Bradbury, 30, has a rare genetic form of Alzheimer’s
SWNS

This isn’t how it was meant to be. Five years ago Alzheimer’s was about to become a disease of the past.

In 2013 Pfizer was in the final stages of testing a vaccine that could stop the disease as soon as it appeared. In the unlikely event that failed, the US pharmaceutical company Eli Lilly had a competitor that scientists expected would be a “huge step forward”.

As a final back-up, Roche and Merck were set to realise the billions they had also spent on dementia research, with two treatments that made patients, and their investors, extremely excited.

Then one by one each drug reached final testing, and each drug failed. This week Pfizer in effect admitted that the disease had eluded its scientists — by pulling out of research completely. Now the question is what went wrong. Why are billion-pound drugs failing en masse? There are two theories: one is depressing, the other is devastating.

The depressing theory is that the drugs failed because we need to find a way to start treating people a decade or more before Alzheimer's disease even becomes apparent.

The second, devastating, theory is that our entire understanding of how the disease works, based on tens of billions of pounds' worth of research over many years, is flawed.

In 1901 a man called Alois Alzheimer met Auguste Deter, 51, in a Frankfurt lunatic asylum. As she took a forkful of pork, he asked what she was putting in her mouth. "Spinach," she said. He found she couldn't recognise common objects. She had forgotten her husband's name. Dr Alzheimer was fascinated by her. Patiently, he waited five years until she died — then he examined her brain. He found dead and dying cells, with sticky clumps between them. Today we call these sticky invaders amyloid beta.

Ninety years later, in an article in Science, a young British researcher called John Hardy wrote about an investigation into this protein. "Our hypothesis is that deposition of amyloid beta protein . . . is the causative agent of Alzheimer's pathology." Since then, the "amyloid hypothesis" has been the leading explanation of the disease — and the big money for drugs has gone into those

that worked to stop, or remove, the amyloid.
But the drugs don't work. So where does that leave the hypothesis?

"This has been a very disappointing two years," Professor Hardy, who now works at University College London, said. "Maybe I'm delusional but I don't think many people think amyloid is the wrong target. What we do think is perhaps we need to give the drugs much earlier."

For a decade or more, amyloid will build up without any obvious symptoms. He now thinks that that is when the drugs are needed, and that by the time symptoms appear the disease is unstoppable.

"If you're in the middle of a stroke people won't say, 'Take a statin'. It's the right drug, but too late." His concern is that if companies abandon the drugs already made, "we could miss out on the statin for Alzheimer's".

Carol Routledge, of Alzheimer's Research UK, agrees. "We should test these molecules in much, much earlier cohorts of patients. By the time you see cognitive impairment, the resilience in the brain is no longer there."

For Bryce Vissel, professor of neuroscience at the University of Technology Sydney, uncertainty about the condition is the key problem. As far as he is concerned, the past five years have shown not necessarily that we need to get patients earlier, but that we need to return to basic research. "To solve the complex riddle of Alzheimer's, theoretical models must expand beyond amyloid as the central cause."

Rudolph Castellani, of the University of Maryland, has described the amyloid hypothesis as "too big to fail". "There is too much

personal and financial investment," he said. He argues that, ordinarily, drug failures on this scale would lead to a serious reassessment — could it be, for instance, that amyloid is not a cause of the disease but a symptom?

But there is no sign that this will happen. "Some variation of the same construct will inevitably continue, until some major breakthrough, by accident or otherwise, shifts the focus," he said. Professor Hardy, of course, disagrees. He is also not about to join the counsel of despair. "I'm worried people will pull out even though they have the right drugs in hand — because they were tested in the wrong patients." Are things bleaker than they were? "Five years ago I was telling people we'd have a drug in five years. I'm saying exactly the same thing now. I'm exactly as hopeful as I was then. Of course, people might be less inclined to believe me."

Case study: Father has dementia aged 30
Daniel Bradbury went to his GP in September after concentration problems cost him his job. He learnt he was in the early stages of Alzheimer's. He is 30.

Mr Bradbury, who has 18-month-old twins, is one of the youngest people in Britain to have the disease diagnosed.

In 1999 his father, Adrian, died aged 36 from what he now knows was a rare genetic form of Alzheimer's. That meant there was a 50 per cent chance of him having the gene. The same coin toss will pass to his twins, Lola and Jasper.

The former aerospace engineer said that he now wanted to live long enough to ensure that they had good memories of him. Before his symptoms worsen he hopes to take the family on holiday. He and his partner, Jordan Evans, have set up a charity page to raise funds.

Aunt Agatha
One of the best written and most informative articles I've read in a while - factual and unsensational - thank you.

Sue Bee
In view of this remark that “we need to find a way to start treating people a decade or more before“, ensuring that the population has an adequate level of vitamin D in the body may be a start. Vitamin D helps to maintain normal cellular functions, and prevents the onset of a number of diseases such as Alzheimer’s disease, diabetes and hypotension to name three, but there are others.

Sue Bee
That should have read hypertension!

Mo Lindt
"Castellani... has described the amyloid hypothesis as “too big to fail”. “There is too much personal and financial investment,” he said."
So - this is about money.
But I am interested in health. And we know by now how to treat Alzheimer and how to reverse it!
Check out the American neurologists Dr. David Perlmutter and Dr. Terry Wahls.
Try changing your lifestyle, your diet first and do exercise! Modern life as we know it makes us sick. It has to change.

https://www.drperlmutter.com

Bryan Dale

Billions spent on huge research projects with no results. Maybe what is needed is smaller expenditures on smaller companies that may give a fresh look at this and other diseases.