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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Alzheimer's Disease: What's The Latest Research?

Dr. Lisk:
Although there is still no cure for Alzheimer's disease, we've made great strides in understanding this tragic disease that affects more than 50 million people worldwide. That's why today, we're taking a look at the latest updates and the progress we've made in treating and alleviating this disease.

You're listening to *NeuroFrontiers* on ReachMD, and I'm Dr. Jerome Lisk. And joining me to talk about what's new in Alzheimer's disease research is Dr. Peter Whitehouse. And with him today is Dr. Daniel George. They are both co-authors of *American Dementia: Brain Health in an Unhealthy Society*. Additionally, Dr. Whitehouse is Professor of Neurology at Case Western University. He is also a Professor of Medicine at the University of Toronto. Dr. Whitehouse, welcome to the program.

Dr. Whitehouse:
Great to be with you and with Danny.

Dr. Lisk:
And Dr. George is a medical anthropologist and Associate Professor of Humanities and Public Health Sciences at Penn State College of Medicine. Dr. George, it's great to have you with us.

Dr. George:
Likewise. Thanks for having us, Dr. Lisk.

Dr. Lisk:
So let's just dive right in. Starting with you, Dr. Whitehouse, can you explain some of the current developments in Alzheimer's research?

Dr. Whitehouse:
Yes. I think there's a lot to say, Dr. Lisk, but the most important thing I think is that Alzheimer's is not one thing. It's now known to be a syndrome. Parkinson's experts know there's overlap between Alzheimer's and Lewy body dementia, and we know there are vascular risk factors. So when people say that Alzheimer's is the most common cause of dementia, they should not be referring to it as one thing. And in fact, the most common cause is a mixed pattern of dementia with vascular factors as well as Alzheimer's type changes.

Dr. Lisk:
And with that being said, in your book *American Dementia: Brain Health in an Unhealthy Society*, Dr. George, can you comment on Alzheimer's research that you address in the book?

Dr. George:
Sure. I'll pick up where Peter left off, which is the sort of nature of the condition we're dealing with. It's not one single disease. It's a heterogenous, age-related syndrome. And so, when you think about curing something that is syndromal, it sort of is resistant to single-mechanism drugs, and that's what we've seen for the last several decades and even more profoundly in the last year with aducanumab, the anti-amyloid drug, that these single-mechanism drugs just haven't worked. What we're dealing with is a very complex syndrome that is resistant to these sort of reductive approaches. But what has worked—and I know we'll touch on this more later—is the sort of public policies and public health measures that we put in place in the 20th century. Those have driven down Alzheimer's and dementia rates not just in the United States but in Canada and four other Western European countries over the past several decades by 13% per decade for dementia specifically and then 16% per decade for Alzheimer's disease. There's a really interesting story underlying those trends that we'll touch on later.

Dr. Lisk:
So Dr. George, with that being said, and when it comes to our research efforts, what are we doing right and what are we doing wrong?

Dr. George:
Yeah, I like to start off on what's going right, and what I find in my own work—and I have my medical students go into local nursing homes around our medical school—we do a lot of work with the arts in dementia care, so this is things like storytelling and music and pet therapy and expressive artwork and intergenerational activities, things that really connect to some quintessential element of what it means to be human. And people with even advanced memory loss can engage in these sorts of activities and have their quality of life improved by virtue of participating in them. And I think what we've done right is start to look beyond reductive pharmacological approaches and think about, you know, what is it about our shared humanity that might be the basis of "interventions" or just basic human activities that we can bring into these assisted living environments. And I hope that we continue to fund more of those efforts moving forward.

And that juxtaposes nicely with what we've already sort of alluded to as to what we're doing wrong, which is these single-mechanism reductive approaches to try to reverse the pathologies of Alzheimer's disease, which are, again, complex and heterogenous and age-related. And I think Einstein, of course, is famous for saying that insanity is trying to do the same thing over and over again and expecting different results, and that's a bit what it's felt like to be in the Alzheimer's field for the last two decades where we have had over 40 anti-amyloid drugs universally fail at the cost of billions of dollars, and hopefully, we'll learn the lesson in the wisdom of thinking outside the amyloid box as we move forward, but I think that's kind of in a nutshell where things have gone wrong.

Dr. Lisk:
Let's come back to you, Dr. Whitehouse, and take a closer look at Alzheimer's drug development. From your vantage point, are we doing a good enough job of identifying therapies?

Dr. Whitehouse:
No, I think we're not, partly because of this fixation on amyloid we've already talked about, and this is why, as Danny and I both said, aducanumab is not the right avenue. And in general, we tend to focus too much on molecular or pharmacological fixes. The field is being driven by biomarkers, this idea that we can diagnose Alzheimer's disease with a PET scan, or now there's a great focus on amyloid blood markers. The field wants to make Alzheimer's disease a biological disease that you almost don't need to talk to the patient and family about because you just walk in and do these biomarkers. So I think this is usually damaging to the humanity of both the patients and for that matter, the skills of neurologists who are important to the diagnostic process.

The other thing we have to be very careful about is the idea that this is completely separate from aging. It's not. There are terms that are controversial, like mild cognitive impairment, that tells us that to one degree or another people suffer from cognitive challenges as they age, so that's another aspect of research that's so important. And finally, because it's related to age and because when you can damage your brain at any age, it's important that pediatric and geriatric neurologists band together and talk about brain health and prevention, across the life course.

Dr. Lisk:

Amazing. For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Jerome Lisk, and I'm speaking with Drs. Peter Whitehouse and Daniel George about current updates in Alzheimer's disease research.

So Dr. George, now that we've reviewed some of the latest research and therapeutic developments, I'd like to switch gears a bit and focus on the prevalence of Alzheimer's disease, because, as I understand it, dementia rates in the US and other Western countries have fallen in the past decade. I know you mentioned this a little bit earlier in the program, but can you do a deeper dive and give us some insights into why this may be the case?

Dr. George:
Absolutely, and this is the most exciting thing happening in Alzheimer's world in my opinion. So I mentioned before, the rates are falling in the United States but also in five other countries, and when the data for those countries has been pooled, there are two main patterns that emerge from the data. One, as we've sort of touched on is that there's been better prevention and treatment of vascular disease over the last 50 or so years, and there's also been an increased access to education, especially at a higher education. And so, when we zoom out from that research, we need to ask what's happening in these Western countries across the 20th century that is now sort of precipitating these benefits for people who are aging into their grand years and experiencing less risk for dementia.

We passed the G.I. Bill, which gave access to tens of millions of veterans to higher education. As did the competition with the USSR, which expanded state universities in the United States, and Pell Grants, which obviously invited more people from disadvantaged backgrounds to access higher education. So the education side has been profoundly improved in the United States and these other countries but also vascular health, as I mentioned. All the countries except the United States, where we're still struggling to provide healthcare for everybody, passed national healthcare systems in the 20th century, and that increased access to to care for things like hypertension and diabetes and high cholesterol, things that we know affect the health of the vascular system and thus the health of the brain.

I'll just mention two other things which have emerged in the data; one being the enormous success of antismoking campaigns in the 20th century. So in the 1960s, over 40% of the country smoked. Those rates are down to about 14% today, again making a major impact on vascular health. What's good for the heart is good for the head. And then de-leading gasoline, which we started to do in the 1970s under the Clean Air Act, it reduced blood level rates of lead in American citizens by 80% from 1970 to the 1990s, lead being a major neurotoxin but also a risk factor for heart disease, so getting that out of the environment made a dramatic effect on brain health.

Dr. Lisk:
Okay, now, turning to you, Dr. Whitehouse, what strategies are needed to continue this decline?

Dr. Whitehouse:
Danny and I have talked about mental exercise and education, but in Parkinson's and Alzheimer's, the value of exercise on brain health cannot be discounted. It not only keeps your heart healthy; it keeps your brain healthy.

Brain health is important for people with all kinds of neurological disease and other diseases, and it's been a great pleasure in my career to work with people like you who focused on Parkinson's disease. We learn a lot from each other, and we learned that these diseases are much more complicated than we think; single-drug approaches are not likely to work—although we've made much better progress in Parkinson's than we have in Alzheimer's—but in terms of curing or fixing these diseases, we need to focus on public health, physical exercise, and engaging people in things that improve their quality of lives as they get older.

Dr. Lisk:
That's very impactful.

Well, you both have brought up some very good points and some things that I think many of us have not thought of before. And as that brings us to the end of our program, I want to thank my guests, Dr. Peter Whitehouse and Dr. Daniel George, for joining me to share their insights on Alzheimer's disease. Dr. Whitehouse, Dr. George, it was a pleasure speaking to both of you.

Dr. Whitehouse:

Thank you.

Dr. George:
Thank you, Dr. Lisk.

Dr. Lisk:
For ReachMD, I'm Dr. Jerome Lisk. To access this and other episodes in our series, visit reachmd.com/neurofrontiers, where you can Be Part of the Knowledge. Thanks for listening.