



Alzheimer's, Dementia, COVID-19 Long Haulers, and Other Brain Disorders

Cheng Ruan, MD
with **Dale Bredesen, MD**



Cheng Ruan, MD

So today we're gonna talk about memory and Alzheimer's and have a very special guest on, he is the author of the End of Alzheimer's and this is Dr. Dale Bredesen. Dr. Bredesen received his undergraduate degree from Caltech and his medical degree from Duke. He served as president and chief resident in neurology at UCSF and then was supposed doctorate fellow and the laboratory of the very famous Nobel laureate professor Stanley Prisoner. He was a faculty member at U. C. L. A. And in 1998 became the founding president and the ceo of the Buck Institute for Research on aging and the adjunct professor at UCSF the brightest in laboratory studies, basic mechanisms behind neurodegenerative disease processes and the translation of this knowledge into more effective therapeutics and tactics for Alzheimer's disease and other neurodegenerative conditions.

This led to a publication of over 220 research papers and he established the Alzheimer's drug development network with Dr. Vargas in 2008, leading to the identification of new classes of therapeutics for Alzheimer's disease. So him and his group developed many different approaches in the latest actually is something called the Bredesen protocol described as reversal of symptoms of those people with memory loss, mild cognitive impairment and Alzheimer's disease. And it's a precision medicine based protocol. I was published in 2014 and had multiple enhancements and revisions recently and so honored to introduce Dr. Bredesen to talk about the root causes of memory loss and we're gonna talk about this program called recode and we're gonna talk about how this is really applicable to people with all sorts of neurodegenerative diseases. And of course Alzheimer's disease. I'm so excited to talk to you about cognitive decline and memory is going to be exciting conversation So well welcome to the summit.

Dale Bredesen, MD

Thanks so much, Cheng. So much to talk about. This is a really exciting time.



Cheng Ruan, MD

It is you know we met a long time ago in person and that's when I first heard about the recode approach. And I want to say that's 2,017 we met in Florida And it was one of the 1st 1st lectures on this approach on sort of this reversing kind of decline. So a lot of happens between now and then and uh right since 2017. And this is the most fascinating field of research that I've seen. Just because we're now using things in our language like immune health and diet and things that a lot of neurologists and people just don't talk about. So first of all let's talk about how this precision medicine protocol was developed. It's got taken decades to even think about right?

Dale Bredesen, MD

It's a great point. So actually I started up my lab at U. C. L. A. In 1989. So the whole idea was to understand the fundamental nature of neural cell death. Why do neurons die? Why do you get these degenerative diseases? Why are they so common? And so we wanted ultimately to understand what's causing the problem. And so over the years we started to see a pattern. We started to see that Alzheimer's is not what people were teaching. It's not just about amyloid or just about Tau or just about type three diabetes or any of those simple theories. This is really about a network insufficiency. It's really about looking at an entire system together. And as you know, the big problem with classical medicine unfortunately is that it's now outdated, people are looking at these. It's literally like you're looking at the, the titanic, which is mainstream medicine, you know, has crashed into the iceberg of chronic illness and it's going down right in front of our eyes. And so we've really got to understand people as complex systems. And so we started to see that you could look at the signaling and how it was altered in people with Alzheimer's disease. And you could actually trace molecular pathways into this beautiful system.

This beautiful network and you could see that it's insufficient. So as an example, as a comparison imagine we take the United States of America. Okay, that's a complex system. There are all these things. We take it as it currently is. And now we're going to ramp up inflation to 25%. We're now going to dramatically increase the toxicity. The air pollution is now 10 times worse toxins in the rivers, 10 times worse, everything is 10 times worse than it currently is. Then we start having some invaders coming into the country and starting to wage war on the country and then we deplete the support so that the companies can't do their jobs were not able to do commerce, That's Alzheimer's So in other words it is an insufficiency of a complex now network. So now you can change the inputs to the network. The network starts to crumble and so it can only work as a smaller network and that's exactly what we're seeing in the synaptic networks of people who are developing Alzheimer's disease.



Cheng Ruan, MD

So synaptic network, can you define what that really means?

Dale Bredesen, MD

Yeah, that's a great point. So in your brain you've got this amazing supercomputer of course. So you have about 100 billion neurons and actually you have about 10 times that many glial cells. So you all got also got support. You've got the astro glial, you've got the old God Indra glia which wrapped the myelin and of course, and you've got the micro glia which are there that do the immune part of this gobble up pathogens and things like that. But also secrete cytokines. So you've got this beautiful network where each neuron makes on average about 1000 synapses or so. So 1000 or a little more. So. So basically you've got almost a quadrillion synapses in your brain. It's an incredibly powerful network that you have.

So you've got tremendous computing power. And one of the major things that goes wrong in Alzheimer's is that the synapses start functioning less well and ultimately are lost. And then ultimately of course the whole cell is lost, the neuron is lost. But classic studies by Professor Terry from many, many years ago, a famous neuropathologist showed that what correlates best with the problems and the severity of Alzheimer's is synaptic loss. So that is a fundamental problem. And so the question is why, why are you losing these synapses? Is this something where something is killing them off? And the big surprise is that the amyloid that we make, that's the hallmark of Alzheimer's. This amyloid and tau is the second hallmark is actually a protective response to these various problems. So you put pathogens in someone's brain. One of the things they do is make amyloid to cover and kill that pathogen. And professors Robert Moyer and Rudy Tanzi from Harvard showed a number of you years ago that amyloid beta is actually an antimicrobial peptide.

Now the problem is of course it's not just killing the microbes, it's also downsizing your brain. So it's doing both. But therefore when we want to treat this problem. First of all we want to get in early of course. But second of all we want not to just remove the amyloid. That is an overly simplistic idea that has not worked as you know with multiple approaches. So what we want to do is determine why the amyloid is there. What caused the problem is this insulin resistance is this reduction of trophic factors? Is this specific pathogens? Is this specific toxins you want to determine it for each person and then you want to address those? That's why it's precision medicine because you're addressing the actual causes of the problem and it's given as you know the best results of any approach to date. So the simple point here is all we're doing with recode is identifying and addressing what's causing the problem.



Cheng Ruan, MD

You know it's so complex and as you said there's a bunch of different synapses that's going on multiple multiple ways that it's as being lost right? Whether it's nutrition inflammation toxicities etcetera etcetera. Another segment Speaking with Dr. Daniel Amen we actually talked about how difficult it is to put words into numbers. So to quantify literally you know Yes you know grandma and grandpa has memory loss right? But what is there is there a number associated with the technologies that look at that? Because what we know from M. R. I. S. And from C. T. S. And stuff like that is so limited. So how do we quantify the actual memory loss that someone has. So we know we're kind of going in the right direction.

Dale Bredesen, MD

Yeah I think it's a great point and obviously Daniel's done a great job with not only people with cognitive decline from Alzheimer's, but also things like chronic traumatic encephalopathy and things like that. So you're right and you know this is the future. We will be able to get better and better and better definition of what's actually causing the problem right now. We can get a very good idea by looking at things like how much inflammation, what pathogens are there, what toxins are there.

But for example, we don't have a good simple way to measure intra neuron or or intra brain interest cerebral nerve growth factor. Right now, we'd love to know what that is. I'd love to know what the, you know what the interest cerebral a DNP, another important trophic factor is we can get now a serum BDNF but that again, that may or may not be reflective of interest, cerebral BDNF. This is where we hoped. Exorcisms were really going to be helpful. They haven't proven to be at least early on, they haven't proven to be as helpful as we had hoped. So, there's a lot more to know. And of course the genetics have been, have given us an idea that really gives you an idea about the Proclivities, but it doesn't tell you the current state. So, putting all these things together, we can really get an idea of the Proclivities you have to begin with? Where do you stand? Why do you stand there and what is it that we need to do to get you back to normal?

Cheng Ruan, MD

I wish there was just one test, right? One thing to just look at and boom, magically, we have this sort of, you know, Alzheimer's score and that is not the case and...

Dale Bredesen, MD

That will happen.



Cheng Ruan, MD

It will? You think so?

Dale Bredesen, MD

I think it will, but it will be a nuanced score. It'll, it'll basically be telling you a lot of little pieces to it, but it will be a score that say, here's where you stand and here are all the contributors. So you're right, it won't be one scalar. That's correct.

Cheng Ruan, MD

People are terrified of talking about memory loss. People don't admit they have memory loss and when a spouse or someone talks, calls them out and say you should see the doctor for it. There's a lot of fear behind it because there's this idea in sense that why would I want to know something that I have no control over? And this is a shame because there's a lot of systems of controls that people can establish over Alzheimer's and not just Alzheimer's, but also from neurodegenerative disorders right now. What do you say to people who are just terrified of thinking, man, I have this memory loss, I want to see my doctor, I don't wanna be all doom and gloom. I just want to, you know, keep going in the way that life is going right now and hope for the best. What do you say to those people? Yeah.

Dale Bredesen, MD

You know Cheng, I'm so glad you brought that up. If you could get across one thing to everyone it's that you do have control over this. People have been told it's hopeless and that is no longer the case. That's what we're all showing now every day. And so what I recommend to everybody is think about the four phases you go through and that's presymptomatic. SCl subjective cognitive impairment which lasts about a decade. M. C. I. Mild cognitive impairment and then dementia full on the end end stage. Alzheimer's basically If we can just get everyone to address the first two. So if you get on prevention, if you're 45 years of age or older please get on prevention. And if you don't do that at least at the first sign of anything wrong, do not wait. And you can have tremendous control. And you should never you should never get demented. No one should get demented. This should be a rare problem. It's because just as you indicated, people worry about it, they think it's hopeless. They're told there's nothing in the armamentarium. And so what do they do? They put it off and put it off and put it off and as you know and you've seen again and again there are so many wonderful stories and they're just our recent trial showed this 84% of the people in the trial actually improved. Didn't just slow the decline. They actually improve their scores and so people are seeing this all over. Of course, Dr. Heather Sanderson is showing improvements in her trial as well. Dr. Sharon Houseman Cohen showing improvements her



patients as well and just, you know, your patients as well and on and on and on. So now I think it's up to all of us, we've got to go into all the different areas. What about the people who are very late in the trial? What are about? People were interested in this as a quote Sarah Trial severe Alzheimer's reversal attempt. Is there some you can do for someone who has a MoCA score of zero? We've seen people go now from 18 to 30 a perfect 30. We've seen people go from 0 to 9, we've never seen anybody go from 0 to 30 and I look forward to that day.

Cheng Ruan, MD

Right? So mocA score 10 is really, really bad and 30 is perfect. So we're looking forward to going from really terrible to to really well, I'll tell you. and you know, as you're saying this, let me, let me kind of explain to you a lot of the biggest success stories that we've had here at Texas center for lifestyle medicine when it comes to decline and we're talking about MOCAs from like single digits to the upper twenties. Okay. And so and this is a part of my career I never, ever thought I would ever talk about which is dentistry the one of the biggest aha moments is when we started looking at and working with people in the head of the next space. So Dennis E. N. T. S. Allergists and people like that. We're noticing that there's a lot of hidden inflammatory and immune networks within the skull, right in the skull of course cradles the brain that is not seen. And actually earlier today someone we've been working with someone for three years and it took me three years to convince him to see a biological dentist. They found a very terrible amoeba that's actually in the sinuses.

Yes. And I will tell you that you know post operatively after that was taken out and it's a collaboration between the dentist and Adonis and the E. M. T. And the R. He spoke clear sentences for the first time in three years. And so yes and this is this is you know day one post op and thankfully they were able to do this without general anesthesia. I did a lot of drainage but it's incredible and but I have a lot of these stories that there's a lot of things that are hidden that's outside of my specialty which is internal medicine that when we start collaborating people will start seeing things and as it turns out we went back into the data two years ago, there's this a sleep study that was done in last sleep study done for the patient. And after we diagnosed with sleep apnea. And there's this really weird spike right at the infrared portion of the frontal lobe. And then we didn't really know what it was. But now we know that's a manifestation of something that was brewing there because it's easier. We don't really know what it is. It's some sort of signal abnormality. M. R. I didn't show anything. The cat scan didn't show anything. We kind of just played it off right. And so it's really the dentist that really became the hero the dentist. Like no this is abnormal you know right now.



Dale Bredesen, MD

Is this an amoeba or a Naegleria or something different?

Cheng Ruan, MD

No this is something different actually being under analysis right now. So this is a organism that's similar to tuna Gloria. So what we have found out is that it's not just that it's their spire Keats within the oral microbiome. So there's all these different pathogens that are in there that that now we're going to the dental community and the dental community is reaching out to us because they're seeing these people who have underlying dementia and they're cleaning their their airways and we're seeing that they need entire neurocognitive work up. So I think the collaboration. But and I use Dennis and E. M. T. Is just one of the many people who collaborate with the collaboration I think is really key to tease out these intricacies so we can all you know work together. But I feel that there's so many things that I was not taught in med school residency, right? And I just thought hell, you know, you know Alzheimer's is a disease of too much amyloid being in the brain.

Not realizing it's an immune response is supposed to be there and how we not have the ability to create Malloy, we might be dead, you know, much earlier on. Right. And so and so this is my aha moment for me, for me starting when I met you in 2017 in Florida until now and that progression just gotten bigger and bigger because there's so many things that are out there that's contributing to it. And you know, one thing I really got to say about the rico program is rico program looks at everything, looks at everything from every point of view and it really opens my view of what brain health really is. You know, it's the brain is the body is the skull, it's the it's the spinal alignment, the connections, it includes the liver includes the kidney is such a beautiful thing and the brain is is the transmission of the body where it kind of orchestrates everything and it's it's a beautiful thing to see people improve. But I think it's more beautiful when everyone can stand by and look at this patient and really appreciate what transformation they really have. And then a lot of times a week or two weeks later, they physically look different. They look younger. Wrinkles starts to, you know, start to appear to go away. And it's very transformative to see.

Dale Bredesen, MD

Yeah. And you know, this is bringing together uh you know, traditional Chinese medicine with modern medicine to say, look, you know, what, what can we see here that's actually driving. And so the thing that excites me is that this comes straight from the test tube, all the experiments we did over 30 years. They in this direction so that you can't ignore all these different things that all p



play on that network of neural plasticity. And if you ignore them, you're not going to get best outcomes. I mean, just as you were pointing out with your patient with the Naegleria like organism, you got to get at that and the same thing with T dente cola and ginger Vallis and all these different things that can all play on that neural plasticity. I hope that ultimately it'll be simpler and we'll be able to do some very simple tests. But right now you have to remember this is a terminal illness. So when people begin to have cognitive decline, only one of two things will happen either, you'll figure out what it is and you'll help them and get them sustainably better or they will die. And so you really want to pull out all the stops, Look at all the things, find out what's driving the problem and then address those with a precision medicine sort of approach.

Cheng Ruan, MD

Absolutely. And I think what's beautiful about all this, it's really requires a lot of people to be in a place where it's really patient centered medicine. I think this is how all medicines should be really proud right with the integrative approach. But let's talk about something that no one really likes to talk about, which is like the naysayers because I feel like there's a lot of people that look at the stuff that I do and that stuff you do. Well this is not, you know, a pharmaceutical trial any way, shape or form is not designed to be so and so there is a lot of support from the medical community and there's a lot of naysayers from the medical community like how do you how do you navigate that?

Dale Bredesen, MD

Yes, if it's okay, let me just, I want to address one thing that you said just a minute ago before and then we'll go into the naysayers when I was coming through and this was you know, I'm much older than you are when I was coming through way back in the seventies and eighties. What happened was there were all these specialists, we say, okay we're sending you to a cardiologist because you have a heart problem. Okay, now we're sending you to Arenal Doctor because you have a kidney problem. Now we're sending now what's interesting is you still need all the different people. But now these people are all addressing one problem. It has all these different fingers coming out from this problem. So, okay, you have cognitive decline. We need to know what's going on with your heart, and your liver, and your gut, and your sinuses and all these things. So it's really a completely different way of thinking about medicine, but looking at these systems is critical. So, apologies. Now let's go, let's go back to your point about the naysayers. Yeah, and I have to be honest, I am I've been surprised at how negative the Naysayers have been. But you know, I understand that the idea is if, you know, if you consider yourself an expert and you're doing something the old fashioned way, the last thing you want is for someone to come along and say, no, you have to change the way you're doing that. No, you say, wait a minute, I'm the expert. I don't have to change the way I'm going after Amyloid because that's what experts



do. I'm gonna go to meetings on Amyloid, I get grandson. Amyloid. I talk about Amyloid, I study Amyloid. So if you're telling me that, that's not the answer here. I don't want to hear that. And so, you know, it's kind of funny. It's sad for the patients. However but you're you also alluded to the trials? Yes. We'd love to have a you know a phase three trial for everything. But that costs many many millions of dollars. Some of these uh you know some of these trials are 50 \$100 million for a phase three trial. So what we really want do is start with the science. How does it actually work? Get some preliminary data? Look at anecdotally. Can we actually make people better? I thought when we showed for the first time and published back in 2014, hey here are people who are reversing their cognitive decline and then hey they're sustaining. People would say okay great let's try this and let's see if we can make it better and better.

But the response was we just don't believe it. Well okay talk to the patients, look at the data whatever you like. So we've just kind of the next step next step. We've had 10. Then we had 10 with better documentation. Then we had 100 anecdotally. Then we just published just recently the trial in the Journal of Alzheimer's Disease. And this is where we took a proof of concept trial, 25 people who had well documented M. C. I. Or dementia and showed that we could make them better, 84% of them improve their scores and so now we're taking the next step which is a randomized control trial and I'm very, I'm very honored to be doing this with some absolutely outstanding positions with at six different sites. So we're doing this with Dr. Anne Hathaway here in California, Dr. Kat Tubes in the East Bay, Dr. Christine Burke in Sacramento, Dr. Craig Tanya in Miami, Dr. David Haase in Nashville and Dr. Nate Bergman in Cleveland. So very excited to be working with six absolutely outstanding positions. And that's gonna start later on this year.

Cheng Ruan, MD

That's amazing. And where do you see this going? I mean, you have your collecting this data. Like what would be like the best case scenario for getting people to understand that there's a reverse ability to a lot of the symptoms of cognitive decline. Getting people to say that, hey, hope is okay. We just have to have a very standardized approach to it. Like how, what is that suppose to go in the next five years or so. It's a great point.

Dale Bredesen, MD

So there are different pieces to this immediately. The important thing is public health. So what we want to do is reduce the global burden of dementia. This is a huge, you know, this is a trillion dollar problem globally that affects so many families and destroys families and destroys everything the families have done together. It's really sad. So that's the key thing to get it out there to get it into standard of care because as you know, the standard of care today, you go into a memory and aging center, they're the experts. They take a small data set, they give you a drug



and they tell you you're gonna die. It's very very sad. It's really now an outdated approach. So the first thing is public health. The second thing then is to begin to simplify, can we do things that will make it so that it's easier for more people to do this? And then the third thing is to now make this better science and more. Can we now determine what are the critical variables? My hope is in the long run we'll have equations. We currently use a computer-based algorithm. But over time as we collect data will be able to put numbers on there. So we can say to someone 27% of your cognitive decline is due to this infection in your sinuses. 28% is due to your insulin resistance. You know, 15% is do that. And then we'll be able to adjust each of these things and see people get back to normal and then stay normal. We have people now who have been on the protocol for over 10 years. The first people started 2012 and they've sustained their improvements. But we have others that have often going off where they haven't sustained their improvements.

So we want to make it so that everyone can sustain their improvements and we can tell them here's what's actually causing it then of course to be able to adapt this for all of the other neurodegenerative illnesses. And we've started as you know with what we call the Ark Project A. R. K. Just like two by two by two animals. The idea is to look with small numbers of patients with a larger a deeper dive larger data sets and see if we can also reverse those. And actually we started the first patients in Texas and we have some dark adaptation with people with macular degeneration showing that we can normalize their dark adaptation improving their symptoms from macular degeneration. So very excited about that. I want to be able to show the same thing with A. L. S. With Frontotemporal dementia with Lewy body disease etcetera. So and we've already seen good results with Lewy body disease with our protocol. But I think all of these can be adapted to get best outcomes from these other currently untreatable illnesses.

Cheng Ruan, MD

So but the question is why? Because I feel like in the medical community we have diagnosis codes that are very secular when it comes to a lot of brain health. Right Well not just brain health mental health as well, you know you have anxiety and you have A. D. H. D. You have etcetera etcetera. And the because of these diagnosis there's stigma to them as well. So a lot of people in the public I feel like they want to know exactly what they have for an exact solution, but a brain how there's so much overlap. And so what so I guess my question to you is yes, we know that in Alzheimer's disease, there's just how protein is amyloid. That's a hallmark feature, bits immune response. What about all these other neurodegenerative diseases? What are the commonalities there? And what are the differences?



Dale Bredesen, MD

That's such a good point, you know? So here's the interesting thing and this is now, you know, at the conceptual level, how can we take this to the clinic and get improved outcomes? Because these as you know, these are all virtually all been untreatable illnesses. So the concept here is the same for all of them. The idea is neurodegenerative disease is due to network insufficiencies. So you have a network that's important for neural plasticity, you have a network that is important for motor control and that network is what's being what's failing in parking disease. You have a network that it's important for motor power, that's what's failing in a l s of course, support of your macula, that's another one that's what's failing in macular degeneration, PSP progressive, super nuclear palsy is another one. That one again is a cousin of Parkinson's but unfortunately untreatable with with typical Parkinson's drugs. Again, it has the same sort of achilles heel, which is energy related as does Parkinson's.

So for each of these, you're looking at an insufficiency of a different neural sub network and so we can define that insufficiency. And it's really interesting because each of these sub networks has its own achilles heel. As an example. Anything that causes mitochondrial complex one to fail is going to increase your risk for Parkinson's or Parkinson's related syndromes like PSP or M. S. A. Things like that. On the other hand, you look at Alzheimer's and we know the common things, insulin resistance changes in oral microbiome as you pointed out sleep apnea, things like that changes in oxygenation. That's all part of the energetic that are critical for this neural plasticity. So each of these sub networks is different interestingly in A. L. S. It's really about glutamate uptake because you've got this severe this excited toxicity as Professor Professor rothstein showed many years ago from Johns Hopkins. So each of these things has a different set of problems and a different achilles heel. And we can therefore define the network for each of these and determine what's going wrong and address those things.

Cheng Ruan, MD

But so each of these achilles heels is really depending on what set of network malfunctions I guess there are within the brain. But one cause can affect any of these networks right.

Dale Bredesen, MD

Exactly. And it's just you know, some some people again partly because of their genetics you know two people will go out and get exposed to uh you know to to uh you know air pollution. and insulin resistance. One of them will develop Alzheimer's the other one will develop Parkinson's. So yes, there are these various genetic predispositions as well, but these things all contribute to network insufficiencies.



Cheng Ruan, MD

You know, another part of this stuff that we actually talked about headaches in general. And one of the things that we talked about was there's so many different types of headaches, cluster headaches, migrants, etcetera, etcetera. And then the conclusion was, well, you know, one something can trigger any of these headaches. They just have pretty names to them based on the diagnostic criteria. So we're talking about the same thing in neurological disease, right. Yeah.

Dale Bredesen, MD

And when I practice neurology, I treated a lot of people with headaches and you know, what we would always do is this a tension headache? Is this a migraine? You know, is this something different? Is a cluster headache? What is it, define what kind of headache it is and give the appropriate drug for that kind of headache, but we virtually never knew. Well, so why are you getting a headache? You know, what's going on here? Uh And so, you know, now again, this is 21st century medicine, It's not about what it is, what's the diagnosis, It's about why it is. What are all the contributors is do you have uh an amoeba in your sinuses? Do you have uh you know, do you have oral problems. And do you have something else?

Cheng Ruan, MD

Right. And uh you probably don't have a Motrin deficiency or something like that causing it? Right. Yeah. So, a lot of things that we were taught especially in medical school are sort of these band aid things that yes, we're gonna take care of the patients and make them feel better and put them on the back. But you know, looking at the root causes a whole different, you know, phenomenon, not just in genetic diseases but all diseases and disorders, right. You know, another thing that I really struggle with and you may not know, this but ever since 2017, majority of what I do on a clinical basis now is pretty much like neurology at this point because of the success of what has occurred in the last five years in terms of what we learned from recode in terms of you know, everything in the collaboration and the practice, my struggle and I want you to I specifically want one of you on this summit to ask you this phenomenon. We noticed that a lot of times when the patient actually gets better, they become more aware and therefore more depressed into the family. It may seem that they're more withdrawn or maybe they're they seem more demented but in reality on Euro contesting they're actually testing better. Can you speak to this phenomenon?

Dale Bredesen, MD

It's a great point and I know in Marama the assisted living facility Heather had mentioned a patient as well who clearly was better cognitively but then started ruminating more and saying



gee you know what am I doing here in the world and that sort of thing. So but here's the thing, there are a couple of important pieces to this. Yes you've made this improvement in their performance. They are more aware as you mentioned. But there was some interesting work from Yale a number of years ago from a professor who showed that we've always think of depression as being a depletion in serotonin. But her argument was you can argue equally well that it can be an over abundance of acetylcholine. So we're pushing on these people to have a greater Colin ergic tone because that is so critical for memory.

So we're giving them things like alpha GPC and citic align. And even sometimes things like who present a and things like that we are improving their colon ergic tone. One of the unfortunate side effects of that is you may get someone who feels a little depressed because of that improved coal energy tone even though they are performing better. So what you want to do is now you've got to bring the other corollary systems up. You know the complementary systems you've got to make sure their dopamine is good enough and make sure they're Norepinephrine is good enough as well. And so that's part of it. The other thing Yes, you do get some insight and also you're, you know, you're struggling to to improve even more. So I think the important point is don't get discouraged by that.

You're clearly on the right track, you just haven't arrived at the destination yet. And so the thing that I always tell people get tired of hearing it, I always say to all the patients when I'm talking to them, please keep optimizing because that's where you're going to get the best outcomes in the long run. You know, good example, someone get some improvement now they backslide a little and we find a ha something's been missed. Now you improve that and now they get even better improvement or someone says, well I'm not complying as well as I used to because you know that and better, that's all I need for now, we'll know keep on going. You may be able to get better and better and better. So again, we're defining the neurochemistry of synaptic function so that we can make it better and you may have little hiccups along the way, like a little backslide or compliance issue or a little depression uh and just keep on keep on optimizing and you'll get really good results.

Cheng Ruan, MD

Right? And I do want to address that, you know, shout out to a lot of the caregivers listening to this because it is a tough job trying to manage your own life. Plus your loved one, it is very, very tough and we recognize that right? And so and the reason I asked you about, you know, when people get better, they start getting depressed is that the caregivers suffer a lot of guilt looking through that process uh that yes, yes, the memory could be a little better and the functioning a little better, but you know, he or she is more withdrawn uh seems to not talk as much, not be



more interactive and there's a lot of guilt that really comes when when people, you know start to get a better process but I agree with you just have to like keep going and then the other part I think is there's a fear of false hope. Not just from the caregivers but from the patients themselves too right? And as the patients become more aware of their surroundings, of the people that are there and they become more constantly understanding. The patients themselves have a guilt because they, the patients themselves feel like they're a burden for their family and their caregivers. So it's like a bidirectional, you know guilt thing that a lot of times we have to just you know, council and overcome and that's that's you know, it's great that we're seeing people get better but for me that's probably the toughest part to to to to to help manage and help people, you know meet the expectations, you know.

Dale Bredesen, MD

And I would argue that there is a lot of false hopelessness. I mean, yes, I understand people always say false hope, the reality is there is now a lot of false hopelessness in cognitive decline. So, you know, you go onto a website for a foundation or you go to a memory, an aging center, you go to an expert and they all say the same thing, There's nothing that can be done. Forget it, it's hopeless and that's no longer true. So I would argue that false hopelessness is a problem that is on the increase. Also, you mentioned the caregivers, I think that's an important point. There is such an important part of all this. There's a very interesting paper that's now impressed in Journal of Alzheimer's disease that will be coming out. And it's talking about the health of the caregivers and different responses of the caregivers, some would get angry, you know, some would get verbally abusive, you know, some would just kind of put kind of everything would be shoved under the rug. They tend to get different types of health problems. So we have to take good care of the caregivers as well as taking good care of those who are cared for.

Cheng Ruan, MD

Absolutely, I 100% agree with that because some of our more severe cases and more difficult cases are those people actually without any caregivers. and that they're unfortunately sort of part of the system. Unfortunately, it's really hard to manage those people as well. And uh, and for those caregivers listening to this. If you are supporting someone through any sort of brain issues whatsoever, they're lucky to have you, you got to pat yourself on the back at least once, maybe do it now, you know, uh, and and and understand that, you know, through love, everything can really be accomplished. But I agree with you. Dr. Bredesen the false hopelessness is much, much bigger, I think, and especially what we see. And I'll give you this one story is we have your biggest fan. One of my patients, his name is Carl, he says, hello, He knows we're talking today, and and Carl um, has multiple copies of your book at the end. Alzheimer's multiple. Give it to the church members. He goes on these walks and a couple of years back, he was in an Alzheimer's dot org



walk and um, the staff members respectfully told him not to pass out anything that's related to like the end of Alzheimer's and given this false hope, and I'm just like, cover my head. I'm like, are you serious, Carl? Like, you went out with your church to go on the Alzheimer's walk and they're not gonna let you, like, at least provide some hope for people. And it drove me a little insane. Just kind of hearing that. But that's the that's sort of the delicate situations that we're seeing right now in the public of this false hopelessness. That's their right.

Dale Bredesen, MD

Well, what's interesting is we all want this to be blessed, anything that's new. If you get a new treatment for cancer, a new treatment for Alzheimer's, a new treatment for lupus, we want it to be blessed by the experts. And we always think that the experts are completely objective. But the experts are, you know, they're they're they're being paid by drug companies. They, you know, they're they're they have their own non objective reasons. And so we were waiting for blessings. And so, you know, here you go to this walk and they're like, well, you know, here's what we believe because this new approach, even though, you know, that like read the papers, we've published this, it's in peer reviewed journals, it's happening. Their argument is it hasn't been blessed yet by us and therefore we can't talk about it, which is sad because it is offering false hopelessness, right?

Cheng Ruan, MD

And I think that that validation is what people are kind of, you know, searching for and coming around. Um, but I, you know, I want this summit to really be educational experience for people and having people experience the process themselves and then decide for yourselves, right? And the last thing that I want to go over with you is um, what I've seen ever since the global pandemic hit. So through the coronavirus, I learned a lot about the brain. I learned the the amount of brain issues long haulers and stuff like that, you know, almost called acute onset of Alzheimer's and some people, it's startling and what we're seeing is that if you have something like Alzheimer's that that that gets worse over 40 years, we're seeing that gets worse over three months now with with coronavirus. Right. And so what do you, what do you think you've gleaned from the global pandemic and how it affects the brain right now? And how does that really affect your view of what brain brain health is?

Dale Bredesen, MD

It's a great point. And as you said, you were seeing brain fog everywhere now, so many people, young people and so we're really having to take the same principles that we've used for Alzheimer's And move it basically 20 years earlier for everyone who has brain fog that evaluated. Please find out what are your contributors because, as you know, many of the same things and



here's what's the interesting parallel. There's a lot of parallel between Alzheimer's and COVID-19. Although one is clearly a viral illness and one is much more than just a viral illness as we were talking about it. It's many things that have to do with this. Net, but they have a number of things in common because, you know, for example, you low vitamin D. You're at risk for worst. Covid. Alzheimer's have low estradiol obesity insulin resistance a po E four is another one. All these things just go right down. But what they have in common is in covid 19, you have your innate immune system activated, so you have this inflammation but your adaptive system has not been able to clear. You're supposed to be able to hand this off. Now, the innate system goes down. Your adaptive system takes over.

You now get rid of all that inflammation. You have a very specific approach, cellular humor response and now you clear the virus. Everything is good. But the problem is because of the strategies of the virus itself, your own genetic background and your own biochemical background. You're in a state in which your innate system is still on and your adaptive system is not clearing. So you die of cytokine storm. This just keeps boom innate system. Now in Alzheimer's, what happens is you also have the innate system active and you haven't cleared whatever the problems are. And of course it can be mycotoxins and all these other things, whatever it is, you haven't cleared it. So therefore you don't die of cytokine storm because it's a chronic illness. You die of cytokines drizzle, you just have this chronic ongoing, ongoing innate system activation. And so our job is to find why that is get rid of that and then bring up that adaptive system support the body. And that's where there's a lot of relation between what happens in Covid 19 and what happens in Alzheimer's disease. But I agree with you. It's really making all of us even more aware of optimal brain health.

Cheng Ruan, MD

Silicon Storm versus Silicon drizzle. I'm totally gonna use that. It's a beautiful way of looking at it and really helps me really understand this concept right? whenever we have our patients with any sort of neurocognitive issues and they actually get the coronavirus there is sort of this temporary you know decline, right? And then when they get over it they come back some people come back faster than others. Right? And so I feel like that's the same way with just people developing disease and disorders. There are things outside of genetics that are responsible for how people are reacting to whether it's viruses, whether it's toxins and things like Alzheimer's and stuff like that And so you know we label this epigenetic you know beyond the genetics and surrounding the genetics. What do you think are the top epigenetic factors and lifestyle factors in reducing either the risk of Alzheimer's or improving cognitive health that people listening right now can just start doing at home. Like right now some simple things. Yeah so you bring up a really good point.



Dale Bredesen, MD

So let me just address what you said earlier first and that is this whole issue of getting worse. So you have someone who's now on the upswing they're doing better with their cognition, they're beginning to feel that underlying problem whether it's S. C. I. M. C. I. Or or Alzheimer's they're beginning to improve and now boom there suddenly get covid 19 and they usually take a step back and again because their innate system is now reactivated, their adaptive system hasn't cleared yet. And so you've got this again, it supports what we're all saying about Alzheimer's disease, that that's part of the problem here. So we now want to help them get over this and you yes, they'll often take a little step back. But then in the long run they'll start coming up again and that happens with any info.

I see it with kidney stones, with gallstones, with operations with a lot of anesthesia, with a new infection with new exposure to toxins. As you know, all these things you take a step back and so now you've got to figure that out. Uh And and Julie G, for example, has talked about her own story where she was doing really well. And then it turned out that she had undiagnosed. So to come back to your point though about what are the things that we can do today. The most important thing is to get evaluated because this is as you said, this is a complex situation and so you want to know what are the contributors but I understand, you know, a lot of people their local doctor may not be doing this. You can always get a cog Nazca P. So I recommend everybody please get a cog Nazca P. We all know to get a colonoscopy when we turn 50 if you're 45 or over or if you've had covid please get a cog Nazca pc where you stand. Uh and and be able to address those things.

And it starts with the basic seven things which are diet. You know, you want to have a mildly key to plant rich, mildly key topic. Diet high in phyto nutrients, you make sure that it's anti inflammatory, all those important things. Hopefully omitting grains, dairy sugars, things like that. Uh And then uh you know then any sort of gluten or dairy, that sort of thing. And then exercise. And boy there's there's great stuff on exercise that wasn't around even a few years ago. Things like uh these these katsu bands that have been very helpful and improve muscle mass improving therefore your insulin sensitivity. eh wat exercise with oxygen therapy very helpful especially for people who have vascular components. So lots of important things both on the aerobic side and on the strength training side. And then third one is sleep. And again you could write books on sleep. And of course Professor Matthew walker has done that is as has arianna Huffington and others tremendous amount that you can do to make sure that you've got the right of course wearables are going to help so many of us to see the problems before they ever



come to see whether you have a low heart rate variability or whether you have poor oxygenation at night. That's one of my biggest concerns. Low oxygenation at night affects so many people.

And of all people, I just found out recently it was affecting me. I didn't know this for years. and so okay now I know that this has to be addressed as well uh to avoid problems. And so sleep is the third thing stress management stress a huge issue. You just look at people with high stress and it's been well documented. They have smaller brains. So you, you know, let's reduce that problem. Uh And number five is brain training. Professor Mike Merzenich started this years ago. Fantastic brain HQ has done well for so many of our patients. And then six things are targeted supplementation, all sorts of things and people say well you know, supplements aren't a cure for Alzheimer's. Of course they're not, nobody's saying they are, hopefully, but getting the optimal biochemistry for your brain is huge and they can be helpful. No question about it. And the armamentarium is huge, being able to target the right ones for the right person.

Very helpful. And then the final thing of course is detox and I was never taught as a neurologist that these toxins were causing cognitive decline that we ultimately call Alzheimer's disease. I didn't know about trico these scenes or glia toxin or Okra toxin. A I didn't know that air pollution was an important one. We knew that mercury could be a problem but we didn't realize how commonly this could be associated with Alzheimer's disease. We didn't realize about the organics, the glyphosate and tallulah lines and Benzene and formaldehyde and all these things. So now we are getting a much better kind of crystallized view of what it is that's actually driving for each person. So I recommend everyone. Please get checked out these. There's so many things you can do for yourself and just go by your own outcomes if things are going well. Great. Keep optimizing. If things are not going well, please consult with your practitioner because he or she can help you.

Cheng Ruan, MD

Now. Let's talk specifically into the rico program. So what's it like of being a person going through the report rico program. What's that journey look like.

Dale Bredesen, MD

Yeah. So it's straightforward and trying to make it more straightforward. So you simply you you can go on you can go on my colonoscopy dot com or drbredesen.com or Apollo health code. Any of those and you can sign up for re code. It's simple. We do re code is for reversal of cognitive decline and pre code is for prevention of cognitive decline. So if you're truly uh scoring really well you have no complaints whatsoever then just do prevention. But for anyone who has any complaints or who's concerned or has it running in their family? Please do recode? you can



actually then get your labs directly from online and then you can have, then you have access to trained over 2000 physicians. Obviously you've done a great job with all the people who have come your way so that then we can link with people where you are and we have people all over the world Uh in 10 different countries and all over the us who, you know, who are doing this successfully and getting people to improve. And of course we're all interested in the same thing which is continuing to evolve and get better and better and better as we learn more and more. I'm not, I'm never saying this is the final answer. We're always looking to get better and better and better outcomes. So that's recode pretty simple. Go online, get your blood test, go to a practitioner who knows what he or she is doing and get a good outcome.

Cheng Ruan, MD

That's amazing. And what's really exciting all this is that for those people who go on recode you're using that data to compile even more data for the future. So you can be predictive of what factors cause what and how much and that's the beautiful part behind it. Right. It's not just About, you know, you individually as a person going through it. It's also about the contribution factor to the greater good than to the study of medicine. Study of brain health. What is the perfect age. Is there a perfect age to start either rico or pre code? Yeah.

Dale Bredesen, MD

For anyone who's 45 or over. I would recommend please get on as early as possible. The farther you go, the harder it is to get a complete reversal back to normal as you know. So please get on early as possible. Now one caveat here, 95% of people who develop alzheimer's have as, you know, sporadic Alzheimer's where you have genes that increase your risk, like a P four or various alleles that increase your risk, like a P four uh and others trim too. And there are many of these, but that 5% that has true familial alzheimer's where you have a mutation in a P. P prison in one or prison willing to, they can start earlier. They may get it. Some of these families get it in their twenties. And so whenever, if you are truly in one of those rare families that has it, go in 15 years before the on instead of the symptoms in your family. So if everybody's getting this when they're in their mid thirties going in, if they're getting in their mid forties going when you're 30 now we are dealing with just a few people who have familial alzheimer's and it's in their family and we're seeing some good results so far. But we don't know yet it's it's a different thing because the genes there have such a powerful effect,

Cheng Ruan, MD

Wow, that's amazing. So to think about this from a preventative standpoint and understanding that the earlier you start, the better the outcomes may be is truly inspiring. And I want people to listen to this is that there is a fear behind neurocognitive disorders like Alzheimer's disease. But if



there's something that's out there that can either prevent it or that can reverse some symptoms of it, you've got to be able to just just attach onto that and understand at least what it's what it's about. And you know, not all doctors understand this process and you're right and learn that through med school, you know. Uh and and not all people are going to be want to be part of this process, but that's okay. Sometimes you just have to advocate for yourself and I really want to thank you for writing the first book, the end of Alzheimer's which is one thing that a lot of patients come in, they have things highlighted it and we'll kind of go through, it's actually a lot of fun and we actually had text center for lifestyle medicine.

I did an entire book review of your book in online format mode that we have for our patients on our on our memory programs, so they know exactly what each thing is talking about and it's becoming wonderful. So, for and and people are listening to this. If you if you want a full review of dr Benson's protocol, just go to [www dot tcl m university dot com](http://www.tclm.university.com), scroll down to the root cause of memory loss and I go through in my review of the of the entire book of the end of Alzheimer's and what each of the section is that we can't really cover on this short segment of our interview As well. but thank you for coming on. I mean this has been an incredible talk leaves me with a lot of hope and I hope people listening to this are going to be developing that hopeful mentality of there are things that we can do right now for yourself, for your brain. So thank you for coming on.

Dale Bredesen, MD

Yeah, thank you Cheng. And you know, this is the time for updating of all this, as you mentioned 2017. So that was five years ago. So we're now looking at a second, a second edition of this with updating everything there. As you know, there are tests phosphor Tao Abeyta 42 that weren't available for intra uh you know uh in the blood instead of just the CSF Epigenetic tests, all these things that weren't available even a few years ago. So we'll be able to do better and better with following people and get better and better outcomes. So thanks again Cheng.