You Can Prevent and Even Reverse Cognitive Decline – Dr. Dale Bredesen with Dave Asprey – #754

Announcer:

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Dave Asprey:

You're listening to Bulletproof Radio with Dave Asprey. Today's guest is back for a second time on the show, and he's one of my favorite guests. He's a UCLA professor, and one of the smartest and most studied guys I've ever met when it comes to neurodegeneration and Alzheimer's. I'm talking about Dr. Dale Bredesen, who wrote the groundbreaking book called The End of Alzheimer's, where he just straight-up told us, "Here are the different types of Alzheimer's. Here's what we know, and it is absolutely 100% reversible and preventable. We've solved this problem, but no one knows." He says it from a position that's really hard to argue with because he has all the data, all the science, and he's got decades and decades of practice behind him. So he's very credible on this notion.

His new book that just comes out as we're doing this episode is The End of Alzheimer's Program. So the first book said, "Here's how it works. It is real. You don't have to get Alzheimer's. You can reverse it. You can prevent it. You can be smarter now." This is the book that goes with it that says, "Here is the actual things you do. Here is the lab tests you get." So this was the idea of turning it from science and knowledge into action, and this interview is all about that.

You were the first very, very well-credentialed physician that I know of who put in a book straight-up toxic metals and toxic mold are contributing factors to Alzheimer's disease. Then, you have the data, and you have the studies, and you put it all in The End of Alzheimer's, which just floored me when I interviewed you the first time like, "Wow." The functional medicine side, the things that I know about my own path there, I know that those destroy cognitive function, but you put all the dots together to say, "All right. Let's look at these as things that are lighting the fire, and then how to put them out," which is part of why you just came out with your new book that's based on the program you're actually doing for patients.

Dr. Dale Bredesen:

Right. Yes. We had a lot of people ask after the first book, "Well, hey, we want more details. You've talked about, 'This is feasible. Here are some examples. Here are some anecdotes,' but we want more about where do we go? What are the URLs? What are the workarounds? Who are the people that have done it? All these things. What brand do you want to buy for all these things?" Obviously, you've been through this with Bulletproof. How do you get optimal outcomes? I mean, that's the critical. What are the critical features?

The thing that's been really intriguing to me is that there are so many misconceptions and misunderstandings about this illness that people don't understand what's driving it, so they just, as you said, they just say, "Yeah. We don't know what causes it. There's nothing you can do about it. Forget it." Beyond that, the funny thing is anybody who says different is lying. Well, wait a minute. What about the published data? My argument is once the data are published in peer-reviewed journals, which we've now done multiple times.

Dave:

Yeah.

Dale:

If you don't have something that's that effective, then that's criminal negligence. You're saying, "Okay. I'm aware there are data. They're published in peer-reviewed journals, but I'm going to choose to let someone die rather than using those data." I mean, there's a legal term for that. It is criminal negligence. So it's a crazy time, but I think that the next few years, we're going to see more and more people saying, "Yes. Look, this really did help me." We're just finishing, by the way. We're finishing the trial. This is the first trial in history, and if you think about it, again, it makes no sense. The old way that this was done, all trials up till now have been, "We predetermined what the treatment is." Right? We say, "Okay. We're going to treat you with drug X," or, "We're going to treat you with change Y." Whatever it is, it's a univariable and, "We're going to give you this, and we're going to predetermine it."

Well, that's not really the way the human body works. So what you need to do is say, "We're going to take each person, and we're going to evaluate all of the variables that are contributing to their change." Cognitive decline in our case, but you can do the same thing for longevity, for diabetes, cancer, what have you. We're going to look at all the contributors, and then for each person that's going to be different, we're going to address those variables. When you do that, you get much... No surprise. You get much better outcomes, and you get sustained outcomes because you are addressing those. So I'm enthusiastic this thing is finishing in December. It should be published next year. I'm sure there's going to be lots of screaming, yelling, and kicking, but the patients are doing great. Of course, they're very enthusiastic about it.

Dave:

It actually makes me a little bit relax to hear you talk about it that way from something that I didn't realize was much of a stressor in the back of my mind in some small corner. When I started out, when I'm 300 pounds, no one can tell me why exercising a lot, eating nothing... why I'm still fat and why I felt like crap all the time. No one believes me medically. "Oh, yeah. You're eating Snickers bars when we're not looking. Clearly, you have 10 symptoms. You have hypochondriac. Take some [inaudible 00:05:19]." That kind of go-away perspective.

I felt really exposed because I'm a science engineering guy. I said, "Okay. I'm going to try vitamin C," and I looked at my list of things that might work. I'm like, "Wait. If I trial each of these for three months, I'm going to be a hundred by the time I trial each of them once." Finally, I just got frustrated. Unfortunately, for me, at the time, this was right when I made a ton of money that I lost two years later. In my mid 20s, I said, "Okay. I'm just going to do everything that might work all at once. If I get the result and I have expensive P, I'm okay with it because the result is so precious." I was even in end of life. I mean, I did have cognitive disfunction that's probably related to what someone feel later in life, but I said, "Yeah. How do we get results? So how do we test five variables at once to see if it works?" Then, face criticism, "Well, how do you know which are the five? Where was the assumption that it was only one?"

Dale:

Exactly.

Dave:

It doesn't make sense, but you actually... You're going out, and you're doing this in studies. Yeah, you're going to piss people off, but you're right at the end of the day.

Dale:

Well, one of the most common misperceptions in the entire field is that this system works as a linear system, which is absurd, and it's so silly that these people think... Okay. So they'd say, "If you want to try 10, 15, 20 things, you have to take each one by itself, and then you have to add. If you see no effects from 10 things, then if you put those 10 together, you're going to get no effect." This is not a linear system. Duh, wake up. So my argument is, "Okay. Find a system that works for you. It might take 20. It might take 10. Then, you can take one away at a time. You really want to be scientific? Fine, take one away, and look and see." This is where...

Dave:

It is.

Dale:

Exactly. You can do it more fancy if you want. You can do AI. Do thousands and thousands of people with thousands and thousands of approaches, and then look for patterns. I have no problem with that, but let's start with something that works instead of living and dying with floor effects and with assumptions. I really believe that this field has more misunderstandings, misconceptions, and misperceptions, and myths than just about any other field, and people are dying. These are not just white lies. These are things that people are dying for, and so let's quit thinking that the brain is functioning as a linear system here, and let's look at what actually makes a difference for people's cognition.

Dave:

Yeah. Outside of your new book about the program that, "Here's the steps you take," book, you are interested in a bunch of technologies. Some of which I have talked about on the show, but other restorative, regenerative technologies. What are some of the things that you're looking at that might be effective in just making people more resilient?

Dale:

Yeah, so it's a great point. So you and I talked about eWAT before, which I think has been very interesting. If you look at what Alzheimer's and... I didn't start in functional medicine. I started in the lab, and so I really believe in functional medicine because that's where the lab led us.

Dave:

Yeah.

Dale:

If there had been a functional medicine, we would've had to say, "Well, what the heck is this stuff?" So the fact of the matter is that if you look at the molecular pathways that drive the degenerative process, the most fundamental nature of what's happening to our brains is that this is an insufficiency. Again, when you step back and say, "Wait a minute. Alzheimer's is an insufficiency?" Well, duh. It makes sense. Your brain is involuting because the entire balance sheet is on the wrong side. You've got a demand for these 500 trillion synapses that you have, and you have a supply. As we get a little older, and of course, it can happen younger if you've got certain exposures. It can happen older if you're doing well. But at some point, if you are on the wrong side of that ledger chronically, then your brain says, "I cannot afford 500 trillion synapses. How about 400 trillion synapses?"

You're starting to lose these things, no surprise, and you feel it. If you don't discover why you are on the wrong side of that ledge and reconcile that if you don't discover that and rectify it, then it will continually... be continuing the douse us as we see. Ultimately, you lose your speech, and you lose your ability to care for yourself, and on and on, and you die of Alzheimer's. In fact, 45 million of the currently living Americans will die of Alzheimer's. That's 100 times as many as will die of COVID-19 in the worst projections. So this is 100 times the pandemic. It's not as quick of a pandemic, of course, but over the long haul, it is a huge, huge problem. Therefore, it behooves all of us to find out where we stand, which side of the ledger we're on.

The great news is you have years and years before you have a diagnosis of Alzheimer's, so you have a long time. We recommend anyone 45 years of age or older get a cognoscopy. Find out where you stand. Just like you want to know your blood pressure and your cholesterol, you want to know where you stand with respect to your synaptoblastic versus synaptoclastic signaling. You want to get yourself on the synaptoblastic side making synapses so that you can learn new things, you can do your everyday activities instead of being on the synaptoclastic side, which so many of us are. So over the years, we are losing synapses because of dozens and dozens of different things that we can identify everything from your immune system status to your hormonal levels, to your BDNF levels, to your plasmalogens. All these sorts of things are critical, so that is key. You mentioned, "What can you do things?" I don't know if you've talked about Katsu yet. Katsu is very interesting. Have you tried this?

Dave:

We had the guys from Be Strong on, and Be Strong is related. It's temporary hypoxia, but it's still bit less painful than Katsu. It's very similar methodologies.

Dale:

Interesting. Yeah. So the bottom line is this is an interesting period where we can do so much, and obviously, as a world expert biohacker, you know this better than anyone. We can do so much that is not being done by standard of care medicine. Now, of course, everyone can look at their heart rate variability, and their microbiomes, and their 23andMe, and their ketone status, and their continuous glucose monitoring, and their SpO2 at night. Everything. All these critical things that, of course, we can now pick them up. We have a new app that does this so that you can pick up all these things and see quantified self...

Dave:

What's your new app?

Dale:

It's called ReCODE app.

Dave:

Visit ReCODE app. Okay. Cool.

Dale:

Yeah. So it just looks at these various pieces, and it can follow your nocturnal oxygenation, and follow your ketone levels, and all these critical things. Again, we're dealing with a scenario in which you have a chronic insufficiency. Yes, your brain needs oxygen. It needs blood flow. It needs ketones. It needs other

combustible substrates like glucose and things like that in the correct amount. It needs the lipids. You just go right down the list. There are dozens and dozens of things. Unfortunately, when you go to an expert center for Alzheimer's, they do not measure these things, and then they tell you because they're not looking beneath the surface.

You remember that book Flatland, where these crazy things happened because you can't see the third dimension? So people can appear and disappear, and they get bigger, get smaller. It's amazing. We're in Flatland in Alzheimer's disease. People aren't looking. They're not looking beneath the surface, and so they sell you, "Oh, yeah. We don't know what this disease is." Well, if you bother to look in that third dimension, you can see what it is. It is an insufficiency if you know your plasmalogen status, and you know your mitochondrial status, and your [peroxys 00:13:39] level status.

The great news is, just in time, we're all now getting the tools to measure these things. Of course, the doctors who are ahead of the curve are also looking at these things. So you can go today and find out your mitochondrial status. You can go and find out your plasmalogen status. That's now available. Thanks to Dr. Dan [Goodnow 00:14:01], an excellent biochemist who's done a lot of interesting work on plasmalogens and Alzheimer's disease.

Dave:

He's going to be on the show soon.

Dale:

Ah, fantastic. Awesome. It's a great idea. He's a great guy. So there are so much quantified self that we did not have before that I think we are going to see dementia become a relatively rare condition.

Dave:

Wow.

Dale:

We're getting to the point where it's basically a choice. Yeah. If you don't want to do anything, then yeah, you might get it. But if you want to make sure that you don't get this, you now have the ability to do that the vast majority of the time, and that's to me really excite...

Dave:

How long? When is that going to happen? How much time is it going to take?

Dale:

Well, what I can say is today, if someone is asymptomatic or minimally symptomatic, come to us. We can make sure that you don't get it, and that's the vast majority. Now, we'll see.

Dave:

Yeah.

Dale:

So we just released a new program called PreCODE, which is Prevention of Cognitive Decline. So we won't know for sure for the next few years how many of these people will in fact be successful with

prevention, but here's what I can tell you. We've been doing this for a number of years anecdotally, and I've asked all the doctors I talk to who are doing this, "Have you ever seen anyone who went from asymptomatic to dementia while on the prevention program?" The answer is no. So we haven't seen it yet. There may be some people that it happens to, but [crosstalk 00:15:32].

Dave:

Yeah. You'll see it, but it's because of traumatic brain injury. They'll hit their head, and they'll...

Dale:

Yeah, I know, and you're right, and there are other things. Again, this is not a unidimensional problem.

Dave:

Right.

Dale:

This is multiple things, and so you are... You're protecting that huge cache of 500 trillion synapses. Yes, you smash your head enough, that's a problem. You're right.

Dave:

It's one of those things though. If you only get 99% coverage, I think you can consider it just one of the great achievements of, really, the century because dementia has been an issue for a very long time and has since became a much bigger issue in the second half of the last century. It's getting worse and worse now, and so the demand for what I do to prevent is actually big enough that we all know someone who doesn't recognize you anymore.

Dale:

Yeah, so here...

Dave:

No one wants to go there.

Dale:

Great point, and so here's my prediction, Dave. Last century, we conquered acute illness, TB.

Dave:

Yeah.

Dale:

Even towards the end of the century, even HIV is much better, less much less of a problem than it was, of course. TB, diphtheria, pneumococcal pneumonia. We conquered those. By 21st century, we'll see I believe the... and essentially making very rare all of these complex chronic illnesses: Alzheimer's, Parkinson's, PSP, just go right down the list. Lupus, rheumatoid arthritis. All of these things because they are fundamentally different than 20th century diseases and people kept trying to do the same thing. We're just going to throw another medicine at them.

But now, things are changing, and we're able to see what these things actually represent. We're able to look outside Flatland and see what's actually going on, and so we will able, I think, to make all of this rare. Now, yeah, you'll occasionally... As you said, there are going to be people who hit head their head, and you may see some of these. Although, even now, there will be options like stem cells and things.

Dave:

Yeah. You can grow it back. I hit my head hard. I had documented toxin-induced brain damage from toxin mold that Daniel Amen found. It's not there anymore. It does grow back. You can grow it back. I just didn't have a program like yours to do it. I had spent a huge amount of money and tried everything on the planet because I was desperate. So the fact that you've systematized it and legitimized it so people don't say that someone on the ReCODE program is crazy was... Most people say, "Dave, what you did was crazy." I'm like, "Yeah, but 20 years later, look at me."

Dale:

Yeah, yeah. Crazy like a fox.

Dave:

Okay.

Dale:

Yeah, but it works. So the bottom line is we're seeing improvements in electrophysiological parameters.

Dave:

Yeah.

Dale:

You can look at things like P300. You can look at things like dominant alpha rhythm, theta/beta ratio, improvement in PET scans. You can look at changes there, improvements in MRI volumetrics, improvements in MoCA scores, MMSE, CNS Vital Signs, BrainHQ.

Dave:

Oh, yeah.

Dale:

I mean, just write down the list. So this is not someone seems like they're better. They are showing quantifiable objective improvements.

Dave:

As an example out of that list of metrics, my hippocampal volume is 87th percentile for my age. Seems like a pretty good thing, and it probably wasn't when I was younger, but I have good data on that just given the history.

Dale:

Yeah.

Dave:

My P300D is average for a 20-year-old.

Dale:

Wow. Okay.

Dave:

So something I'm doing is working, right? In fact, lots of things I'm doing are working, and that's the rub there. Some of those metrics I use at 40 Years of Zen when we're saying, "How do we increase voltage in the brain?" Funny enough, when you feed someone fried stuff and sugar, you can't increase voltage in the brain. It's not trainable. But when you feed them the right way and the ketones are present, the mitochondria are functioning, suddenly, you can change neuron firing speed, and you can measure it just like you're talking about. I look at this as... It's just an amazing gift to be able to do it to myself and to be able to take one of the lowest hanging fruit like putting some MCT oil in your coffee because coffee is a low-hanging fruit. MCT oil is a low-hanging fruit. Et cetera, et cetera.

Dale:

Yeah, yeah.

Dave:

I want to know from you though because you've got a program now that did not exist 10 or 20 years ago. What are the lowest hanging fruit? For people who's seen the show right now. So you're going to stop doing three things right now, and you're going to start doing three things right now.

Dale:

Yeah.

Dave:

You only have three of each. Tell me what those will be.

Dale:

Yeah. This is a great point. This always comes up, and so I always say the same thing. The number one thing is to find out where you stand because... and I know that will pop out in a way because [crosstalk 00:20:08].

Dave:

Okay. No, no, no.

Dale:

You got to measure these things. You got to see because here's the thing, Dave. Some people are having these involution, are having this insufficiency because of ongoing inflammation. This is what we call type one Alzheimer's disease, inflammatory, hot Alzheimer's. So if that's your problem...

Dave:

That's what I would be at risk for.

Dale:

There you go, and if that's your problem, you're completely different than the person next to you who has atrophic Alzheimer's. So that's type two, and so you need to look at... and then of course, the two of you are completely different from the third person who has glycotoxic Alzheimer's, from the fourth person who now has organotoxic or biotoxic Alzheimer's on the top.

Dave:

That too.

Dale:

There you go, chemo. So yeah. You had multiple sub-types heading in that direction.

Dave:

Yeah.

Dale:

Then, of course, vascular is the other one. So to say three things you're going to stop doing and three things you're going to do, step one is get things checked out. I would include in there to make sure look at your SpO2. Now, you can do that with the thing called Better. You can do it now with the new Apple Watch. There are lots of ways now. You can do it with an oximeter. Your doctor can lend to you any of those things, and also, check out your oral DNA. Make sure that you don't have a lot of P. gingivalis or T. Denticola because, again, another way to give yourself cognitive decline.

Second thing I would say is to get on to my plant-rich, mildly ketogenic, low carbohydrate, gut-supporting diet, and high fiber. It's all the things that we all... We call it KetoFlex 12/3, but you can do it however you want. But those are the components just looking at the biochemistry, and people argue, "Oh, it should be this," or, "It should be that." Yeah. It's getting your biochemistry to be on a synaptic-supporting and synaptic-productive size rather than the downsize.

You were just mentioning the whole system. Okay. Imagine you had an orchestra, but the person who played the clarinet can only play one note. You're not going to get that orchestra to play really well as long as you've got that one guy who can only play one note. As long as you're eating the fried foods and you're doing all the things wrong, you're making your gut leaky. You're making the inflammation happen. You're doing all the wrong things. Of course, you're also killing yourself because you don't have the right nutrients. You don't have the right phytonutrients, support, et cetera. So I'd say that's the second thing is to get on an optimal diet, which is absolutely crucial.

Dave:

By the way, you said mildly ketogenic, not crazy ketogenic. What about all the carnivore people out there saying that plant fiber is all toxic?

Dale:

Yeah. It's a really good point, and I think, again, that we're coming to a point where people are beginning to realize it's not black and white. These things are not that... The human brain is complicated, and so it's not that every single person will be better with this diet or that diet, so take so far. First, I always say... and I've talked to the groups before. I think what they're doing is fine, but here's what I say.

Dave:

Me too.

Dale:

Publish. Publish the data showing that that made someone's Alzheimer's better. Then, I'll believe it. That will be fantastic. So far, there are no publications like that. Theoretically though, where that makes a lot of sense is in people who have inflammatory problems where you've got inflammatory autoimmune problems, especially those who do have this in part because of plant lectins.

Dave:

Yeah.

Dale:

Of course, Steven Gundry has done a beautiful job about showing this and about showing how he could make his patients better by dealing with those, so it's your...

Dave:

It's chapter one of the book. Your diet is lectins, and oxalates on those plant... I think a lot of people are messed up by plants, but doesn't mean all plants are bad for you.

Dale:

Exactly. That's the thing. So everybody wants it to be incredibly simple. "Oh, yeah. Your brain is simple." No, it's not simple, so try... and the people who do the best, as you know, are the people who keep tweaking. They're the ones that come back and say, "Okay. This thing made me a little worse, but hey, this thing made me a little better. So I'm going to go this direction," which is obviously what you went through. That is the way things work the best. So for most people who have cognitive decline, they will do best when we get them into a... When I say mildly ketogenic, 1.0 to 4.0 millimolar beta hydroxy butyrate. If you like to use a breathalyzer, Biosense is a good example. Above seven on the ACEs score. Preferably, even above 10 times during the day. That is providing the energy that there is a tremendous energy gap that you've got to deal with when you have the beginning of cognitive decline. It starts about 10 years before a diagnosis of Alzheimer's, so you need those ketones. You need that metabolic flexibility. That's absolutely critical.

Now, if your big problem is not cognitive decline, and your big problem is rheumatoid arthritis, and you're 25 years old, absolutely, try ALB for a while. Let's see if that helps because then you're talking about your antibodies. By the way, along those lines, you probably saw incredibly interesting recently showing autoimmunity to type one interferons is a major consideration in severe COVID with poor outcomes. It's about 14%. So one out of seven, but it's the first big new one where people said, "Aha, here is a molecular determinant of why this guy died of COVID and that guy did just fine."

Dave:

Once we know that, there's things you can do to calm that down, right? Although I feel like right now, even though with post-COVID syndrome, we have so many limitations where it looks an awful lot like chronic fatigue, or fibromyalgia, or mitochondrial damage, and many viruses and even bacterial infections, a certain percentage of people don't feel good afterwards. They have to recover, and a lot of functional medicine deals with those people. It feels to me like we have this rich tool set, but in the media, I hear people say irreversible in front of that.

Dale:

Yeah.

Dave:

I just roll my eyes on that and say, "Says who it's irreversible? We have no data that says it's irreversible."

Dale:

Yeah. These are the same people who say that if you have said a hundred years ago, "If man were meant to fly, he'd have had wings." I mean, yeah. Okay. That's not the history of our country or our world, right? We're taking on problems and say, "Okay. How could we? If we were to do this, how could we do it?" I think what's going to happen is just the scenario you described, so someone had a virus or they had a bacterium. Now, they're not recovering. They've got this long-term problem, which is... You mentioned it. We're seeing it a lot in COVID-19.

Okay. So as a scientist, we can break that down and say, "Okay. That really has three major components. It has probably an autoimmune component. You've reacted against this thing. Now, you're picking up and reacting against yourself. It's got probably a microbiological component. You've changed your microbiomes. Yeah, you had this. You had this tremendous insult, and now you're starting to come back. Then, number three, it has an energetic component. That's why you feel horrible. You got chronic fatigue. Okay." We can address all of those things just as you just said. We can go in there. We can improve the microbiome. We can get people back to where they should be. We can measure it along the way.

Dave:

Yeah.

Dale:

We can now find what pathogens are chronic. So many of these things as you know. Things like, really, Lyme disease. They're so good at hanging out for years. Well, okay. That's what syphilis used to do.

Dave:

Yeah.

Dale:

We did great getting rid of that. Okay. We can get rid of these if you still got infections. Then, thirdly, we can improve your energetics. So these things are all assailable, and I think so many... Unfortunately, so many times, when the doctor says to you, "It's all in your mind," what he really means is, "It's not in my mind because I can't figure it out."

Dave:

I always hear that, "It's all in your mind," what it means is, "Don't pay me. Find another doctor." That's how it lands through my filter. I don't want to be disrespectful to doctors because sometimes it is all in someone's mind, but that means it's not actually in their mind. That means that there is hidden trauma, and you should refer them to someone to deal with that with the MDR or whatever. That's not what I'm talking about. I'm talking about someone who's actually sick, and is doing what you say, and they don't get better, and then you blame the patient. That kind of stuff is just not going to work anymore.

Dale:

Exactly.

Dave:

I feel like this idea of putting the patient outcome first is relatively new. It's spreading around and saying that matters more than sticking to a protocol or testing just one thing. Some kind of a shift happened maybe just in the last five, 10 years amongst a meaningful enough percentage of care providers. Then, all of a sudden, patients are now saying, "You know what? If I'm not getting the results I want, it's okay to either try something different, or go to a different specialist, or ask for a different treatment plan." Whereas before, there was the white lab coat syndrome. Why do you think that shift has happened, or do you even think it happened?

Dale:

Yeah. I think it is happening, and I think it needs to continue until the standard of care is helping these various people.

Dave:

Wow.

Dale:

As we all know, the standard of care is helping very few people who have complex chronic conditions.

Dave:

Yeah.

Dale:

It is fantastic for a broken leg. It is fantastic for pneumococcal pneumonia. That is what our medical system does very well. There's this old joke about the guy who goes into the doctor, and the doctor says, "You're a jerk." He says, "Well, I'd like a second opinion." He says, "You're an idiot." So this is the problem. People go get these second opinions because they are needed. I think that's where they are valuable. The sad thing to me is the doctor who is the standard of care doctor will criticize the doctor who's getting much better results and saying, "They don't know what they're talking about." Well, then how come the patient got better when they didn't get better seeing you? I think that this is where the... It's the outcome that determines how good of a doctor you are, not where you trained. It's whether you're making people better.

Dave:

Are you going to do stem cells? Have you done them?

Dale:

I have not done them. Of course, I've looked into as many I have and especially because of our interest in cognitive decline,

Dave:

Right.

Dale:

But of course, as impacts on immunosenescence and immune support, impacts on all sorts of inflammatory things, effects on senescence in general, on vascular status, on tumor formation. It goes on and on, and on, and of course, on youth. So absolutely. It's something in my future. Probably next year. If things started looking better from COVID-19, probably next year. One of the reasons I was interested in your history of this was just because are you more interested in autologous, heterologous. In general, I like the idea of starting with the autologous because they tend to do... They have fewer risks, obviously. You're not bringing something from outside. On the other hand, they tend to be things that you can't do as repeatedly as much as often as you can, obviously, with heterologous. So my general approach would be start with autologous and move to heterologous.

Dave:

There's three camps that I've run into around stem cells, and one of them says, "Take your own stem cells and use them when they're fresh." You might get 25 million or something stem cells out of the normal fat aspiration, but it hurts to get that fat taken out.

Dale:

Yeah, it's not... In fact, it hurts a lot more than getting the stem cells themselves. Then, if you're going to do that more than once, how many invasive procedures with liposuction do I want? So then, you would want to culture yourselves, let the weak ones die, and grow the stronger ones, and then put a couple hundred million of your own cells back in. But that's not allowed in the US right now.

Dave:

Also, the question is, what are you losing over time as you're passaging these things through?

Dale:

So yeah, I think there are... We're still in the early days of optimizing this as we are in so many of these things, as we are with neurodegenerative diseases, as we are with longevity. All these sorts of things, and I think this is why this is such an exciting time. These things are all being discovered in real time.

Dave:

One of the things that I'm concerned about... and I want to check and see if you are seeing the same thing I am. It used to be that I could go, and I could google for Alzheimer's disease and maybe alternatives, or Alzheimer's diet, or anything like that, and I would get a set of what people are searching for or what's written about in all of that. I feel like over the last year or two, I do that, and I get straight-up, very traditional, very limited information. The things that I have relied on to write my books to save

my own brain, they're invisible on Google. But I go to a different search engine that actually shows the same thing to everyone, and all the good stuff is still there. I feel like even a work as big as your book, it's getting pushed down by the standard of care by algorithms that I don't want. In fact, I stopped using Google as my search engine because of it.

Dale:

Interesting.

Dave:

Are you seeing that it's harder for people to find or even hope that Alzheimer's can be fixed?

Dale:

That is so interesting. So as you indicated, SEO is such a big issue now, and the problem is that people manipulate the system. Yeah. I'm sure you saw The Social Dilemma, a fantastic documentary about... As they say, if you're not paying for the product, you are the product.

Dave:

Yeah.

Dale:

So many of these issues are about, "Can we now take?" Now that we've gotten past the first wave here, it's all about now manipulating that system, which is really sad because the system was working better without manipulation.

Dave:

So much better.

Dale:

Oh, yeah, but it wasn't enduring to the benefit of people who were paying money. I mean, it's crazy. So I do think we're due for a new time when these things start to come out more, and I think what's going to happen is over time, these will become, because of their better outcomes, they will become the new standard of care, but who knows how long that's going to be? There was just a grant announced in last couple of days to look at AI in various things related to cognitive decline. So what they're saying is there was $17.8 million from the NIH. Okay. What are we going to do? We're going to look at the MRIs, the imaging. We're going to look at the biochemistry, and we're going to look at the cognitive scores.

Well, okay. There's nothing about treatment. We're just going to do the next correlation. Of course, you know about ADNI, the Neuroimaging Initiative, which has been going on for many, many years. Dr. Weiner did a fabulous job with that and those data shared, which was fantastic. Well, this is just the next version of that. We're going to correlate some more stuff, and we're going to hope that the AI will then give us an answer. So we're going to the Oracle and hoping because that's today's flavor.

Well, okay. 15 years and $100 million from now, they'll have what we've been doing for the last few years. We can see the correlations. We can see the improvements. So I think more and more correlation, and this push, this exclusion of anything other than what we got the grant for has really harmed a lot of people. Again, I go back to criminal negligence. When you've got something that is actually helping people and you refuse to use it, is that not the definition? Isn't that negligent?

Dave:

I think it is, and I know how lucky I am that I was successful as a young person. I could dig myself out because I used to hang out in rooms full of people who were completely broke because they spent everything they had trying to get well because they knew that something was wrong, and they could barely get up, and people didn't believe them.

Dale:

Yeah.

Dave:

You start following the threads and unraveling what's going on. You realize every one of those people can be helped, but they can only be helped if people believed that it's possible.

Dale:

Yeah.

Dave:

What you've done, Dale, that really I appreciate is your first book, The End of Alzheimer's. You just laid it out. I think a lot of listeners did read that book. Guys, if you haven't read Dale's first book, this tells you in no uncertain terms we know what's happening, and we know what to do about it. So you can go from, "Ugh, I don't know. Maybe. It seems all complex," to, "Oh my god, we've cracked the code." But then, the next step, which is the new book that you just came out with, The End of Alzheimer's Program, which is, "Okay. Now, you believe from the first book," which is a seminal work for Alzheimer's and cognitive decline. Now, you're saying, "Okay. Here's what to do."

If you don't do both, it actually is a little bit tough because now everyone believes. They're excited, and they're seeking, but they don't exactly know where to go. So doing the work of creating a program I think is harder. At least for me as an author, it's harder to put that together than it is because it's an act of teaching versus sharing knowledge than it is to do the first book. Can I run a hypothesis back to you or past you, something that I've noticed over and over, and just get your clinical and research take on it?

Dale:

Absolutely.

Dave:

It feels like for everything in biology that the slope of the curve of stimulus is the key, and it's why high-intensity interval training, it works better than constant thing. So the flashing lights. On, off, on, off. So it's a very steep curve.

Dale:

Right.

Dave:

Katsu, intermittent hypoxic training, breathe periods of time, no oxygen, deep breathing exercise, cold therapy, heat therapy. It seems like how fast can you heat up the body or cool the body?

Dale:

Right.

Dave:

Even how quickly can you go from a stress state back to a rest state? So can I have a very short spike and come down? It feels like that's the key to almost everything here. Even with blood sugar. Can you have some and go up, go back down?

Dale:

Right.

Dave:

How important is that, the slope of the curve for anything in the brain, or is that too vague of a question to even make sense?

Dale:

No, it's actually a really good point. So some of these is hormetic, as you mentioned.

Dave:

Yeah.

Dale:

You're suddenly cold, sudden hot, things like that, but here's the trick. Yes, it's helpful to have this sudden change because your body responds to that just like with heat as you mentioned. It's responding to that in a regenerative way. However, here's the key. You have to be careful not to exceed the threshold. When you go from hormetic stress to destructive stress, you've really hurt yourself. So here's an example. Go on heat. You keep doing it till you die of an MI.

Dave:

Yeah.

Dale:

You don't want to do that obviously. You want to be careful. So the whole idea is work up to it. That's the key. Now, with the 40 hertz, that's because of specific brain wave frequencies that seem to be... The 40 hertz seem to be an important frequency for support...

Dave:

It's turning off beta or beta almost.

Dale:

Exactly.

Dave:

Almost. Yeah.

Dale:

Exactly.

Dave:

Okay.

Dale:

Yeah, as opposed to driving a different frequency like a delta. That sort of thing.

Dave:

Okay.

Dale:

So each one has something different, but as you mentioned... By the way, as you probably know, they've looked at sound. Guess what it turned out? Around 40 hertz turns out to helpful again, so there does seem to be that something very critical about that particular frequency. So each of these things for a different reason does seem to be helpful, but whatever you do, make sure that you don't do it to the point that you're actually damaging yourself. Again, it's just like people who run marathons get in good shape, but destroy their knees, so be careful.

Dave:

Right. One of the guys who's been copying my stuff for years got into the cold therapy and was like, "I have the air conditioning on all the time, and I'm always cold." I'm thinking, "That's the very definition of not getting it, the brief exposure, and it's over-training." It is basically what it is whether you're talking about any of these things. So I have learned that recovery after the stress is the most important thing. How do people recover best if they don't want to get Alzheimer's?

Dale:

That's a great point. So the first thing is to minimize stress during recovery. So don't drive it so hard that you're not going to recover. Depending on what they're recovering from, stem cells may be part of what's needed, and then there we go right back to where that may be something helpful. Then, making sure that you're recovering to the... What you want to do is you want to recover to the point that over time, you're able to do more the next time. If you're able to do less and less each time, that tells you you're damaging something. If you're not making any improvement, something is wrong. But if you're finding that you... and allow enough recovery so that the next time, you're actually able to do a little more than you are building. You are developing more resilience, more support, and therefore, you're going in the right direction.

So again, with cognition, you can test yourself. You can do things like CNS Vital Signs or Cogstate, or there are all sorts of things you can do, and BrainHQ is a good one to look at, "Am I doing better?" We looked at this in the current ongoing trial, and you can see the people who are doing this more and who are training themselves more, doing overall better over time. So on the other hand, if you

are in a degenerative state, then you're actually going to be going downhill as opposed to going. So simply apply in that criteria. It can help to tell you, "Am I allowing the appropriate time for recovery?"

Dave:

I use heart rate variability from my Oura Ring as my highest and best measure of that. Is that the best one for the average listener to know if they're over-trained, or are there other metrics that you like better?

Dale:

I think that's an excellent one. Again, I think nothing beats ultimately your scores and good function itself. The other thing would be elasticity, vascular elasticity. Again, this is something that things like Katsu address and will improve.

Dave:

Pulse wave analysis basically.

Dale:

Exactly. Yeah, exactly.

Dave:

My algorithm show I have 24-year-old blood vessels when I look at my elasticity.

Dale:

Wow, wow.

Dave:

So something in here is working because I do track that amongst others, and that's a clinical thing you do in the doctor's office, but they put you on a curve according to age and all. For me, that matters a lot because my work with the DNA company, Mansoor Mohammed came on. He's like, "Dave, you're in the top 7% of risk for cardiovascular disease based on a bunch of genetics stuff." So for me, if I look at the big four killers from [inaudible 00:43:28] book, the first step to living a long time is not dying.

Dale:

Yeah.

Dave:

So the big four were cancer, cardiovascular, diabetes, which is a precursor to everything else, and Alzheimer's. Those are what's going to get most of us, and it's funny to me when I look at your End of Alzheimer's Program. The side effect of that, Dale, is that your risk of all the other things goes down dramatically too.

Dale:

Absolutely, because you're addressing physiology and you're optimizing physiology. Again, it comes back to the fact that so many of us are living a very suboptimal physiological life, and that's the issue.

Dave:

What if clinicians want to incorporate your work into their functional medicine practice? Is there a separate side of training? Is there a certification? How does that work? Because to get this knowledge out there, you need coach-type people who can help people be compliant. You need doctors who can get people on the program. How far are you on creating that kind of change?

Dale:

Yeah, great point. So we are and we have created a community. We train 1,500 physicians in 10 different countries and all over the US, and we've just come out with a new training. So this is ReCODE 2.0. That just come out in the last week actually, and then we've got some fantastic people, people I know that you've interviewed before. So Neil Nathan is on there.

Dave:

Oh, beautiful.

Dale:

He's really good, as you know, the world's expert on biotoxins.

Dave:

Yeah.

Dale:

He and Dr. Schumacher, and then we've got Chris Shade, who's fantastic with chemotaxins. So yeah, great stuff with these guys we're doing. Cyrus Raji, who's a word-class neuroimaging person for cognitive decline. Ann Hathaway, who's a BHRT expert for hormone replacement, and then just on and on. So we've really got an all-star cast doing the teaching for this new ReCODE. So you can go on drbredesen.com or any of those sorts of things and just look up for My Cognoscopy, any of those, and look up the new training.

Dave:

All right. There are many, many leaders in functional medicine and practitioners who listen to the show in addition to hundreds and thousands of people who aren't practitioners. So for you, if you're listening, and you run a practice, this is the future, so you might want to look at that training. I don't have a deal with Dale to say that. I'm just pretty good at reading the tea leaves here, and you've done...

Dale:

Thanks, Dave.

Dave:

A very great act of service in putting this up together in a useful, usable format because it's frustrating. So many clinicians that I've known, even going back to my first [inaudible 00:46:08]. Well, everyone had pieces, everyone had a program, but you've done enough of the quantification of it and making the measurement stuff that you do in your cognoscopy. But for people who didn't hear the last episode with you, can you talk about what a cognoscopy actually is, and what it looks like, and why it probably isn't as painful as people imagine?

Dale:

Yeah, that's a good point. Cognoscopy is a lot easier than a colonoscopy actually despite its sound. This comes back to the theory. Once you have an accurate theory, as you know, you can make all sorts of predictions, and that's really what the contribution from the lab was to say, "Okay. This is the theory that tells you why these things have failed, why you have to do this to make it work, and guess what? It predicts accurately who's going to get better and who's not going to get better." That's the whole thing that the lab taught us.

So what you want to start with, as you said, is to get a cognoscopy. You want to know where you stand, and we recommend anybody, 45 or older. You can certainly do it younger, but for sure, if you're 45 or older, please get a cognoscopy. You can do this at mycognoscopy.com or any of the trained physicians. So this is a key thing to do, and you simply want to know three things. Basically, you want to have a series of blood tests. So you want to know what your inflammatory status is. What are the critical features going forward that could increase your risk for atrophic status? You want to know what your omega-3 ratio is. You want to know all these varied... vitamin D status, and your various hormonal status, and your atrophic factors. All those sorts of things. That's all part of this. You want to know your HOMA-IR. Critical thing to know. Very important because you...

Dave:

What was that one?

Dale:

HOMA-IR. This is insulin resistance. It's probably the best measure of insulin resistance, and it's simply your fasting glucose times your fasting insulin divided by 405.45. So you do that, and you'll get yourself a HOMA-IR. You want to be 1.0. once you start hitting 1.3 and above, you have insulin resistance, and we get people all the time two, three, four. These are people with very significant insulin resistance, and it's a very common problem. It predates any pre-diabetes. It predates type two diabetes. So it really gives you a good look relatively early on. So you want to get that series of blood tests that we have in there, that whole set, and then you want... The second thing you want to do is you want to get a simple online cognitive assessment.

We like to use CNS Vital Signs, but there are others you can use. You want to get that as a second piece to see where you stand. We've had a number of young people recently do this, and they were shocked to see that, "Hey, things weren't quite as good as I thought they were," and, "Hey, guess what? I actually do need to." These are people in their late 20s like, "Oh, wait a minute. Yeah. Maybe those Twinkies weren't as good for my brain as I thought they were." So that's that. Again, this is an issue.

Dave:

You think you're bulletproof when you're young, but you're not.

Dale:

Yeah, yeah. Exactly, exactly. Then, the third part is if you have no symptoms and if you're scoring well on your cognitive assessment, then you can forget about the third piece, which is an MRI with volumetrics. However, if you're not scoring well on the test or, and/or you have symptoms already, you want to include that third one as well because you want to know where your hippocampal volume stands. By the way, we've got a woman just writing up who's improvements in her hippocampal volume,

improvements in her PET scan, just striking along with... She went from 9th percentile in her cognitive testing to 97th percentile. She's now 76 years old.

Dave:

Wow.

Dale:

So just doing absolutely great. So those are the three things. That's a cognoscopy. It's relatively simple. You don't have to drink any funny green liquid ahead of time. You don't have to do anything like you have to do for a colonoscopy. It's not uncomfortable. Get those three things checked out and reduce your risk. Let's all make Alzheimer's the rare disease that it should be and can be.

Dave:

Well, I'm on board with that as well. In fact, we just have the virtual Biohacking Conference, right, right before we recorded this. Maria Shriver came on, and she runs The Women's Alzheimer's Movement.

Dale:

Yeah, yeah.

Dave:

Because the conversation went really well, I actually made an additional donation to her charity for that, and that leaves to one of the final questions on the interview just because I know you've got time restraints. Women get two-thirds of cases of Alzheimer's disease. What's different in your new book specifically for women, or do we know what to do that's different for women?

Dale:

It's a great point, and the biggest difference... and of course, the woman's brain is different than the man's brain. Obviously, there are books written about this by Dr. Prisentine, for example, among others. There are differences, and of course, one of the obvious differences is estrogen receptors within the brain.

Dave:

Yeah.

Dale:

It looks as if at least one of these suggestions, and this I think comports well with the data out of Mayo Clinic that showed that people who had an early oophorectomy, so someone who lost her ovaries at the age of 40 or younger who did not have hormone replacement doubled the risk for Alzheimer's, even though the Alzheimer's was diagnosed years later, which again goes perfectly with what everything you and I have talked about here.

Dave:

Yeah.

Dale:

So just a few minutes ago, you talked about the slopes of the curve, and guess what? That is critical for this phenomenon. Now, we talked about how you make things better by changing the curve, and then boom, letting yourself recover. But what about when you do the opposite? What about when you basically knock the legs out from under a system? Right?

Dave:

Okay.

Dale:

So suddenly, and we see this again, and again, and again. In fact, part of what we did with Alzheimer's came from receptors we discovered back in 1993. We published this in Science and Nature of something called dependence receptors. These are receptors that are in many cells, but especially in brain cells that are monitoring the concentration of trophic factors, hormones, things that are trophic to the body. When you suddenly remove the ligand, these receptors actually trigger cell death. So if you're a man, what happens as you get older is that your testosterone goes down slowly year by year, by year, by year.

Dave:

Yeah.

Dale:

The slope of the curve is negative, but it's not negative infinity, right? It doesn't just stop, right?

Dave:

Right.

Dale:

On the other hand, when you're a woman... Now, some women sail through it, and they don't have these dramatic drops. But for many women, as you know, the slope of the curve is much more negative.

Dave:

It's a cliff. Yeah.

Dale:

It's a cliff, and we already know from the Mayo studies. If it's a cliff in 40, you're in trouble. You've doubled your risk for Alzheimer's, so this is where... We also know, by the way, you change that by giving BHRT. Guess what? You lower your risk. So that also...

Dave:

Who would've thought?

Dale:

Yeah. Who would've thought? Yeah. So again, it all fits perfectly with the idea that this is an insufficiency, and we can measure all the different molecules that contribute to this signaling network. We can see why an insufficiency occurs, and we can see what to do about it, and when to do about it,

and how to do it with appropriate treatment. So again, if I were entering that period... Now, I'm much older than that. But if I were entering that period as a woman, I would seriously consider talking to a world-class BHRT expert like Dr. Ann Hathaway, or Dr. Prudence Hall, or one of these other people who has worked with this for years, and years, and years.

Dave:

Well, thank you for saying that, and what I'm hearing there is that it's likely that perimenopause and how that hits you in menopause may be a contributing factor into why women get it more than men because it drops off more quickly and men grinds down over the decades. But for both men and women, having the hormones of a healthy 35-year-old improves quality of life and all-cause mortality risk goes down. It seems like it's a good idea for anti-aging. Are you on testosterone, and do you take those things?

Dale:

It's interesting. I've checked my levels in the past, and at the time, it was fine, but you're right. It's time to re-up this. I am not currently taking testosterone. Although, interesting. My pregnenolone is low, so I take some pregnenolone. So it's [crosstalk 00:54:38].

Dave:

Oh, so you're taking precursors? Okay.

Dale:

Precursors. Yeah. So yeah. So my pregnenolone was low even in my 50s, and so I'm taking some pregnenolone. Absolutely. So these are... Yeah, these are critical things, and I should add progesterone. Women typically have relative progesterone deficiency and relative estrogen excess, and start going through perimenopause and menopause. What is progesterone critical for? Detoxification among other things. So there's another reason that as they begin to lose this, they have increased risk for cognitive decline.

Dave:

Wow, so double whammy.

Dale:

Exactly.

Dave:

So they get fewer abilities to remove toxins, and they're getting slow death because they don't have enough estrogen floating around, or in this case, they have a lot of estrogen floating around.

Dale:

It's not. It's actually lower estrogen, but it's more lower, and so it's a relative excess [crosstalk 00:55:27].

Dave:

Oh, got it. So it's low, but the ratio is even worse? Okay.

Dale:

Exactly. It's a double whammy.

Dave:

It's a complex system. Okay.

Dale:

Yeah.

Dave:

Well, we could go on for hours, and I think people would listen for hours, but I know you have another appointment coming up here. There is far more in your books than we could possibly today including just the list of labs people should be getting. So thanks again for your life's work on this and being the first guy to stand up and say, "Seriously, Alzheimer's is reversible. Why aren't we all doing it?" and then putting the program in place. I'm always in awe whenever we have a chance to talk. So just keep doing what you're doing for a very long time.

Dale:

Thanks, Dave, and you as well. I'm excited about all the great stuff you're doing, and thanks for having the guts, the courage, and the ability to jump out there and to let so many people know that it's a new world. So this is great, so thanks. Let's all make Alzheimer's a rare disease.

Dave:

All right. It's already happening. Your book, The End of Alzheimer's Program, not just The End of Alzheimer's book, so this is the what-to-do book, is just out, and your website is drbredesen.com, B-R-E-D-E-S-E-N.com.

Dale:

Absolutely. All right. Stay safe, man. Thanks, Dave.

Dave:

Guys, if you like this episode, you know what to do. Buy the book and leave a review. Thank you.