164: Dr. Jill Carnahan interviews Dr. Dale Bredesen on The End of Alzheimer's

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Dr. Jill 00:12
Well, hello, everybody, and welcome to another episode of Dr. Jill Live. I'm here with my friend and colleague, Dr. Dale Bredesen. If you have not heard of Dr. Bredesen, you are missing out. But today, I promise you, there are going to be some exciting updates and things. Everything has to do with Alzheimer's disease, preventing and reversing Alzheimer's disease, and cognition. So let me give you a brief welcome, Dr. Bredesen. Thank you for coming on today!

Dr. Dale Bredesen 00:42
Thank you so much, Jill. It's always great to talk to you.

Dr. Jill 00:44
To you too. Dr. Bredesen is an Alzheimer's and neurodegenerative disease researcher and the foremost authority on the reversal of cognitive decline for those experiencing Alzheimer's symptoms. Having spent his career on the forefront of research into the mechanisms of neurodegenerative disease, Dr. Dale Bredesen and his team at the Bredesen Lab have discovered effective therapeutics for Alzheimer's disease. And yes, you've heard me right. Often, we think of recovering from cancer or from autoimmunity, but rarely have you heard how people can achieve recovery or improvement with Alzheimer's. And today, we're going to dive into that.

Dr. Jill 01:22
These discoveries from Dr. Bredesen have led to the publication of over 200 research papers as well as the development of the Bredesen Protocol, a multi-step approach designed to reverse the effects of subjective cognitive impairment, mild cognitive impairment, and early Alzheimer's disease. The protocol is offered through two programs: The Precode for prevention and the Recode for reversal. Dr. Bredesen is also the author of two New York Times bestsellers, *The End of Alzheimer's: The First Program to Prevent and Reverse Cognitive Decline* and *The End of Alzheimer's Program*.

Dr. Jill 01:56

Again, welcome, Dr. Bredesen! It is so exciting to talk to you. And you've got some new stuff we're going to talk about at the end—ways to not only achieve wellness and reversal of Alzheimer's but some really practical tools your team has been working on to help patients achieve even more. I'm super excited about that. For those who don't know you, give us just a little backstory on: How did you get into this research? And where did this all start?

Dr. Dale Bredesen 02:21
Yes, so I came through very, very classical training way back in the 1970s and 1980s through Caltech and MIT and actually spent some time at Harvard on the neurology service there and then at UCSF, ultimately becoming a professor at UCLA. And the idea was that as we came through this, I realized there's nothing you can do about these neurodegenerative diseases. If you have ALS, you're going to die. If you have frontotemporal dementia, you're going to die. You know, if you just go right down the list, it's the area of greatest biomedical therapeutic failure. So I thought at the time, "Okay, I need to go into the lab and start looking at what actually drives these processes."

Dr. Dale Bredesen 03:02
So we spent 30 years, as you said, and we published over 200 papers on what actually drives the problem. And the interesting thing is that it went against what I had been taught. I had been taught that this was about "misfolded proteins." "It's about prions," and "it's about reactive oxygen species." And what it turned out [to be] is actually much closer to what my wife, who is an integrative physician, had told me. She said: "Whatever you guys find, it's going to have something to do with sleeping, eating, and kind of the basics of life." And I said: "No, no, no. We're going to find one molecule with one fold. We're going to get a drug that goes against that fold, and everything's going to be great." It didn't turn out to work that way.

Dr. Dale Bredesen 03:44
So what we found, interestingly, is that Alzheimer's disease is a network insufficiency. You have this beautiful network of about 500 trillion synapses in your brain. And you have a supply and a demand. You need trophic support, blood flow, oxygenation, glucose and ketones, metabolic flexibility, and all these things. And of course, as you have really pointed out with such an expert approach, the toxins you're exposed to, like biotoxins, are absolutely crucial. So we realized, "Okay,

there's this network, and you have to identify the areas of the network that are failing and then you have to address those." And you want to address the things that are actually causing the problem. Sure, downstream, it's fine if you need a drug to change the processing of APP, for example. Fine. But the idea of using that as a monotherapy simply has not worked.

Dr. Dale Bredesen 04:50
And you know, Jill, one of the most interesting and telling things that's come out is the downstream look. So people who went on Aricept or Namenda did worse in the long run than [those who were] going on nothing. People who went on anti-amyloid antibodies, like lecanemab and things like that, have more rapid brain atrophy than people who don't. So these things are short-term, not very good solutions with lots of side effects and huge costs that lead to worse outcomes in the long run. But when you actually go upstream and you look at the various things and you fix the network—and I'm actually writing a paper now on people who got improvements that lasted over five years—we have people [last] 10 and 11 years who have kept their improvements all that time. [This is] something that's unheard of with typical pharmaceutical treatments.

Dr. Jill 05:45
So I love how you describe that because we all go into medicine, and we love the idea of a blockbuster drug that could save the lives of hundreds of thousands of people. But the truth is, it's a lot more complex than that. You just did a brilliant job of describing [this]. You originally put out the research, and you talked about the holes in the roof, right? There are 30 or more. The difficulty is that it's not just one drug or one solution. Unfortunately, it's a lot of hard work, but you've put together a lot of the program to assist and help people. So if someone's at home and they're in their 50s, which is very early for onset—but we're seeing more and more younger people—how could they start? What would you recommend? I know you have something called the cognoscope, right?

Dr. Dale Bredesen 06:31
Cognoscopy. So we're saying, just like a colonoscopy, you should have a cognoscopy if you're 40 or over. We should all do that. But you brought up something really important here. When I was training, we thought of Alzheimer's as a disease of your 60s, 70s, 80s, and 90s. It's turned out to be a disease of your 30s, 40s, 50s, and 60s that just gets diagnosed 20 to 30 years later. So these changes are actually

happening quite early on. This is actually, as you said, complex. But it boils down to two simple things. Number one is energetics—do you have enough? Are you getting enough blood flow, oxygenation, mitochondrial function, ketones, glucose, and those things? And the second one is ongoing inflammation. Do you have a change in your oral microbiome? Do you have exposure to mycotoxins, as you pointed out, and all these things? These are the two big things. So, actually, there is a lot you can do.

Dr. Dale Bredesen 07:34
And you said something really important. We're seeing people [who are] younger and younger. That's been published by epidemiologists. The biggest increases are in people in their 40s and 50s. I've asked a few of my neurological colleagues, way back in the 1980s, when I was training as a neurologist, "Did we ever see people in their 50s with Alzheimer's?" And the answer was "No, we never saw that." One of the most common things that I hear about now [is] a 52-year-old woman. And there are more females because, it seems, of this osteoclastic surge or burst that you go through. It's really been tough because the toxins, as you know, that you're exposed to seem to take a bump at the time when there's this beginning of this osteoclastic burst. So you have that mercury exposure that wasn't so bad when you were sequestering it. Now, it does happen in andropause as well, but it seems to be more common in perimenopause and menopause.

Dr. Dale Bredesen 08:34
So I think what people can do today is get a cognoscopy. Check out [and] see where you stand, and start doing some of the basics. And we think of, as you know, seven basics: Diet, exercise, sleep, stress, brain training, some detox, and some targeted supplements. Those are the basics. And I think in the long run, what we will hopefully have is a public health program where everybody does some basics. And then the people who fall through the cracks and actually get past that—okay, they will then have a more extensive evaluation and more extensive treatment. And then a few of those people will still go through. They'll have to have a still more extensive... As you know, some of these people can be very, very difficult to reverse. And yet you see it again and again. When you do the right things, you see people get better. And most importantly, you see them stay better.

Dr. Jill 09:28
Yes. We talked about, in the beginning here, subjective cognitive impairment—which could happen as early as the late 30s—mild cognitive impairment, and then early Alzheimer's disease. I also noticed you're really framing this. If we have some with very severe or moderate Alzheimer's—at least in my experience, and I'm assuming with yours—it's a lot harder to treat and reverse those patients. So we're actually wanting people to say, "Where am I at?" even if I'm in my late 30s or early 40s. So describe briefly for those listening who maybe don't know what those categories are or what they look like—the subjective, cognitive, mild, and early [onset Alzheimer's]. And then let's talk about what people can do if they're just a little concerned or have a family history. Where can people start?

Dr. Dale Bredesen 10:08
This is a great point. And it's also a common misconception that this is all Alzheimer's. But of course, Alzheimer's is just a pathology. But, as you say, you end up with a [type of] dementia. You go through four phases when you develop Alzheimer's-related dementia. In phase 1, you are asymptomatic. So you go through some period. And sometimes, even in your 20s and 30s, you can begin to show changes in PET scans and changes in spinal fluid. Now, who wants a spinal tap every year? I don't. So the good news is that there is a big breakthrough now with blood testing.

Dr. Dale Bredesen 10:45
You can now get Phospho-Tau 181. If you know your blood pressure and your cholesterol, you should find out your Phospho-Tau 181 and your 42 to 40 ratio of A beta. Soon we will also have GFAP. It's still a research tool. That's even more sensitive, although it's less specific. If your GFAP is normal, you're in pretty good shape because you're not heading for Alzheimer's, at least at that point. So you go through a period that's asymptomatic; that's phase 1.

Dr. Dale Bredesen 11:16
Phase 2 is what you mentioned: SCI, or subjective cognitive impairment. By definition, that means you know there's something not quite right. You're not remembering phone numbers the way you used to. You may have struggles at work or that sort of thing. But you're still able to score within the normal range on

cognitive tests. Now, it may be that you're just really smart, and so you've lost a lot, but you're still able to score in the normal range. But that is SCI.

Dr. Dale Bredesen 11:41
Now, the good news [is that] SCI is completely reversible. We see virtually 100% of those people reverse to normal when they do the right things. And it lasts, on average, 10 years. So you have this clear period. Now the problem is that your doctor tells you, "Oh, it's just normal aging." Please don't listen to your doctor about that, because this is not normal aging. You should not be having this SCI. At the end of the 10 years, what happens is that it tends to convert to MCI. It's too bad that it was named 'mild cognitive impairment'. It's like telling someone, "Don't worry, you only have mildly metastatic cancer." It's a relatively late stage of cognitive decline. And that lasts for typically several years—three to five years. Each year that you have that, there is a 5% to 10% chance you'll convert to full-on dementia.

Dr. Dale Bredesen 12:33
During that time, what it means is that you're now not doing well on the cognitive tests, but you're still able to do your activities of daily living. When you begin to lose those, then, by definition, you've developed dementia. That typically occurs right around a MoCa score of 19 to 22, right in there. So we'd like to catch people when they're up. The best would be when they're up [around] 28 or 29 and still doing very well on their MoCAs, but they just know they have that SCI. Then they do absolutely great. Now the good news [is that] we've had people with MoCA scores of 0, which is end-stage dementia, where they will improve, but they don't improve to 30, which is perfect. They improve to 5 or 9 or that sort of thing.

Dr. Dale Bredesen 13:16
My hope is that we can ultimately understand enough about this disease that we can take people from 0 to 30. As far as I'm aware, no one has ever done that, but that's what we need to understand better. It may take the sorts of intranasal peptides you've talked about in the past. It may take stem cells, or it may take other things. But somehow we need to understand that. But it's a little bit like, at that point, having a collapsed building and saying, "How can we take this now and make it a perfect building again?" We have to figure out how to reconnect those synapses. So those are the four phases you go through.

Dr. Jill 13:49
Got it. And testing this out, where would someone start? Do you offer MoCA online? Or where would people start to get tested? Or would they ask their doctor for a RiCo? Tell us a little bit about [it]. Say someone's out there listening, like, "Oh, my mother" or "myself; I'm having some issues; I'd like to get screened." Where would they go?

Dr. Dale Bredesen 14:08
It's such a great point. And yes, you can just go to mycognoscopy.com, and you can actually get blood tests very easily. You can get an online cognitive assessment very easily. And actually, the online cognitive assessments are even more sensitive than MoCA. MoCA was developed for MCI, but it wasn't developed for SCI. So it's not very good in that SCI range, whereas online assessments like a CQ test and the CNS vital signs... And some people like others, like Cambridge, for example. There are other ways to go. BrainCheck, I think, is another one. These are more sensitive than MoCA, so they can pick up that SCI phase, which is really nice so that you can get things going.

Dr. Dale Bredesen 14:53
And often, as you know, people are shocked. We had one person, for example, who came in even with the MoCA and said: "This is in my family. I think I'm okay, but I better get checked." Her MoCA [score] was 23, which is a fairly late-stage MCI. I'm like, 'Wow!' And she's done beautifully; her MoCA [score] is now 30. She did absolutely great by doing the right thing. So there's a lot you can do by getting started. And the earlier you start, the better off you do, as you know, [as well as] finding the things that you actually have to address. It's very different, as you well know. For some people, mycotoxins are critical. For other people, it's metabolic syndrome. For other people, it's a leaky gut. For other people, it's a change in their oral microbiome. It's remarkable how different the contributors are.

Dr. Jill (pre-recording) 15:41
Hey, everybody. I just stopped by to let you know that my new book, *Unexpected: Finding Resilience through Functional Medicine, Science, and Faith*, is now available for order wherever you purchase books. In this book, I share my own journey of overcoming a life-threatening illness and the tools, tips, tricks, hope, and resilience I found along the way. This book includes practical advice for things like cancer and Crohn's disease and other autoimmune conditions, infections like Lyme or

Epstein-Barr, and mold- and biotoxin-related illnesses. What I really hope is that as you read this book, you find transformational wisdom for health and healing. If you want to get your own copy, stop by ReadUnexpected.com. There, you can also collect your free bonuses. So grab your copy today and begin your own transformational journey through functional medicine and finding resilience.

Dr. Jill 16:37
Yes. This is really at the core of personalized medicine, which is what we all strive to do and what medicine really should [do]. There's nothing unusual about this. It's why we all went into medicine and research to become healers and really understand. But we kind of get the idea that in at least conventional allopathic medicine, there's one diagnosis and one blockbuster drug, like we [mentioned when we] started in the beginning. And it's just not that way. So it's way more complex, but when we get to those root causes that are personalized, we see the really miraculous recoveries that should happen in all kinds of facets of not just Alzheimer's and early cognition issues but other diseases as well.

Dr. Jill 17:14
Let's briefly jump to the mold topic because, as you know, that's near and dear to my heart. I've seen people again in their 30s and 40s with very significant cognitive impairment because of mold. I think one time you said that of the early-onset dementias, you saw around one in three that could be related to a biotoxic environment. Where would you say [it is] now? Would you still agree with that statistic? Or how often is mold a contributing factor to cognitive impairment?

Dr. Dale Bredesen 17:40
Yes, when we were first saying somewhere around one in three or so, we were thinking of the ones where it's the predominant thing. As far as being a contributor, I asked the clinicians that I'm working with on the trial… We have six absolutely fantastic clinicians. I think you know all of them: Dave Bergman, Craig Taneo, David Haas, Christine Burke, Anne Hathaway, and Kat Toups. I'm thrilled to be working with all of them. They're absolutely fantastic. They tell me that in their practices, it's more like 70% to 80% have at least some contribution from toxicity. It's usually mycotoxins; it's usually these biotoxins. That's scary. This is such a common problem. Of course, it's really tough.

Dr. Dale Bredesen 18:26
As you know better than anyone, you've got the spouse saying, "Well, how come I'm doing so well then?" And then you say, "Well, what about the kids?" "Well, one's got ADHD, the other's got a pulmonary problem, and the third one's got this rash." And it's like, "Well, hold a minute. Do you see the pattern here? You are being exposed to things." So it is very tough because this is not even recognized yet. The Alzheimer's Association does not recognize mycotoxins as a cause of Alzheimer's, yet it's one of the most common contributors.

Dr. Jill 18:59
Yes, it's usually insidious because I always say, if I ask patients flat out, "Do you have mold in your home?" 99% will say no because it's hidden behind the wall or floorboard. And it really is an ordeal to figure out what's going on and remediate or fix the problem because often it's hidden, and it can be expensive. So it's hard to get people to go there. But once we test and find out that that is an issue... Now, I tend to work with the younger [age group] with autoimmune [issues] and [those are] environmentally toxic. But cognition is a key component. I think when we look at mycotoxin studies, the number one physical complaint is impaired memory or cognition. So it fits along with that. Again, this could be someone in their 20s or 30s who doesn't have early-onset dementia but whose cognition is really impaired, and even mood and sleep and all of these things that go together.

Dr. Jill 19:48
Sleep—let's talk briefly about sleep because I think this is an under-talked-about topic related to the brain. How important is sleep? How does it affect cognition? And where do you start with someone who's having impairments [in that area] and maybe not sleeping well?

Dr. Dale Bredesen 20:04
Yes, and just to add to what you just said, because I think it's such an important point, there is this phenomenon of younger people having it. So the typical ones we see with inflammation are more, like, in their 60s. The atrophic ones we see who just don't have the hormonal and nutrient support are typically in their 70s. But the ones who come in with the biotoxins are typically in their 40s and 50s, and they do look different. When I first realized this, I was way behind you in realizing, "Wait a minute, hey, there's something going on here." It was because there was a group of people who didn't respond to our original approach of: Let's optimize their

hormones, let's optimize their nutrients, and let's decrease their inflammation. There was this other group. And you're right, they are younger.

Dr. Dale Bredesen 20:53
By the way, as I mentioned, the epidemiologists are telling us that's what's on the rise; the 40-somethings and 50-somethings are hugely on the rise. They're younger, and they look different. They less often have pure memory problems. It's more about executive functions. So I think of non-amnestic presentations. Amnestic is classical Alzheimer's. But then there's this non-amnestic, which is very much what you're often dealing with. Yes, some of them have memory problems, for sure, especially the ApoE4s. But often you'll see an ApoE4 negative who's having trouble at work. They just can't figure out that new iPhone, and they just can't get things together. They can't calculate. They can't make tips. They can't write grants. They can't do all the things that they were doing before. They often have trouble with vision.

Dr. Dale Bredesen 21:40
I was going to ask you about posterior cortical atrophy and primary progressive aphasia, two of the classic presentations of Alzheimer's that are non-amnestic. And they're both turning out to be toxin-related problems. Actually, I was just talking yesterday to Kerry Mills Rutland, who is a health coach and is doing a great job up in New York City. [She is] seeing some of these people who have posterior cortical atrophy, presenting with these visual changes, going to an ophthalmologist and saying, "No, no, this is not an eye problem, this is a brain problem." And it's interesting; they are turning out to be people who have some toxicity. So we're trying to understand: What drives you to have that presentation of Alzheimer's as opposed to a different presentation of Alzheimer's? And they often have depression, as you know. They often have HPA axis dysfunction. They are often exquisitely sensitive to stress. They go on an all-night flight and they're a mess. They often respond quite well to BHRT, for example. So they really look like a different group.

Dr. Dale Bredesen 22:43
Now, my big worry is that we've got all these people who've had COVID; they're all set up for 10, 15, or 20 years down the road to have these same sorts of cognitive problems. So I think that that is an important thing for people to recognize and to get them on [an] optimal treatment [plan], just as you do in your practice. So you

mentioned sleep. So anyway, let me let you respond to that because I think that this is such an important and under-recognized area.

Dr. Jill 23:11
And I want to go on a tangent. We'll come back to sleep in a moment because what you've just said is so critical. I know listeners out there are going, "Yes, I don't feel like I'm quite myself." And especially, I love that you mentioned COVID because what we're seeing is that vascular issues are so prominent if people have multiple episodes of COVID or even one episode. But I see so many things related to hypercoagulability and blood viscosity. And this is absolutely important for the brain, no matter what your age, because probably the number one thing for proper brain function is blood flow to the brain, right? I love that you mentioned that because I think people, post-COVID, are having these long COVID kinds of symptoms. And a huge proportion of that is this fuzzy term called brain fog, which is just that they can't do what they used to be able to do. Executive function—would that be the bucket you'd put it into as far as how to describe the impairment as far as planning, organizing, doing tasks, and understanding?

Dr. Dale Bredesen 24:07
Yes, planning and organizing. Exactly right. And you brought up a really important point, which is this change in coagulability. My colleague and co-author, Dr. Alexei Karakhan, with whom I've worked for many years, pointed out something very interesting: When you look at "Where does amyloid come from?" it is part of the innate immune system. We understand that, but his point was that it's really part of the innate immune system's memory. So once you've been exposed to something, you have a heightened response. And that's basically what Alzheimer's is—this heightened response. That's why ApoE4 [causes a] heightened response to these various pathogens and insults.

Dr. Dale Bredesen 24:47
What happens is that the amyloid is part of a response that lives as the memory in three locations. It lives in your bone marrow, it lives in your endothelial cells, and it lives in your tissue macrophages, which are, of course, the microglia in the brain. So because it lives in the endothelial cells, you lose the ability for this normal laminar flow and this nice flow where you're not having microthrombi. You get COVID, or you're now heading for Alzheimer's; you've now changed your innate memory, and

you're now in a hypercoagulable state. So just as you said, with COVID, you see these multiple microthrombi, which is why a lot of people like to treat it with nattokinase. So you want to get rid of that. And we've had a number of people in the clinical trials where the big problem was hypercoagulability. So this is, I think, a huge and under-recognized area, both for long COVID and for Alzheimer's and various steps along the way, [such as] SCI and MCI to dementia. These are huge and important issues that should be addressed therapeutically.

Dr. Jill 25:55
You've just described it so eloquently because, at the core, it's endothelial dysfunction and damage. And it's interesting because we've known for years that nitric oxide is produced on the endothelium, which is a vasodilator. And when you mentioned women, all of a sudden, in this postmenopause or perimenopause timeframe, that really shifts. That's one of the things where, I think, at the age of 40, we have a 50% [lower] production of nitric oxide than when we were young. And then at 60, it's 15% production. And this is all an endothelial-derived thing that opens up blood vessels and gets blood flowing.

Dr. Jill 26:25
So not only do we have our age instigating a decrease in nitric oxide production, but we [also] have things like viruses—COVID was a big one—and other infections that cause endothelial inflammation and damage. And I love that you're thinking along those lines, because, like I said, probably the biggest thing that I'm seeing now in all realms at all ages is if you had COVID, what that's doing to blood flow, blood viscosity, and endothelial lining. You mentioned nattokinase. Lumbrokinase is amazing. Are you using pycnogenol as part of the main protocol for—

Dr. Dale Bredesen 26:56
Yes, that as well.

Dr. Jill 26:58
And what about nitric oxide precursors?

Dr. Dale Bredesen 27:01
Absolutely. Do you have a favorite one for nitric oxide precursors?

Dr. Jill 27:06
Let's see, Neo40 and Berkeley Life. I really love Berkeley Life lately. They're the ones I've been using.

Dr. Dale Bredesen 27:12
Fantastic. Yes, because we've been using Neo40 in the past. That's a great point.

Dr. Jill 27:16
And interestingly, this is a little point. You probably knew this, but it was fascinating when I found out: We convert the nitrates in our food, like beets, turnips, and leafy greens, with the microbes in our mouths. So when you use those really heavy-duty mouthwashes, you're actually decreasing your body's ability to produce nitric oxide. I didn't know that. So I've been telling people, "Don't use mouthwash if you want that good nitric oxide."

Dr. Dale Bredesen 27:38
It's a great point. It's also why we like things like checking your oral DNA, seeing what your oral microbiome is doing, and then using things like Dentalciden and oral probiotics to optimize. I do think optimizing your oral microbiome is very important.

Dr. Jill 27:54
Yes, because it's so close. And even in the sinuses, when we get mold inhalation, as you know, you can probably describe it far more eloquently than me, but it's so close to that. And we used to think there was no permeability there, right? But as we have infections and issues in our sinuses and in our mouth, it's so close that we do have some transfer across the blood-brain barrier. Any thoughts on that really quickly before we move to sleep? Sinuses, if there's an issue, and the mouth, if there's an issue—why is that important to the brain?

Dr. Dale Bredesen 28:19
It's such a good point. You know, it's been interesting to me that when you look at Alzheimer's, it is largely a face-related brain problem. So, as you said, it's your sinuses, your lips, your herpes simplex here, your change in your oral microbiome, your chronic sinusitis, or even HHV6A probably coming in through your sinuses. We had a person recently with a big fungus ball in his sinuses that had been there and had been missed for a couple of years. So yes, I agree with you.

Dr. Dale Bredesen 28:50
Now, one of the most interesting experiments I read in the last couple of years was where the group was looking to say: Okay, we all know about the blood-brain barrier. It's supposed to exclude all these things. We're going to put Candida into the bloodstream and see how many weeks the blood-brain barrier can exclude it. The answer was a couple of minutes. That was it. So when you have Candida in your bloodstream, it gains access to your brain within minutes. So whatever this blood-brain barrier is, yes, it is great for holding out certain chemicals, but in fact, there are a lot of things that seem to be able to get across there. What do the neuropathologists tell us? P. gingivalis, T. denticola, and P. intermedia are all in your brain. These things are there. And of course, there's more and more interest in these things causing atherosclerosis, distal cancers, and things like that.

Dr. Dale Bredesen 29:44
So I think that this idea that you've got a microbiome and it's kind of stuck in that area—that is going. I'm thinking more and more of us as like the medical internet. The internet, developed by DARPA back in the '60s, allowed us all this communication. Well, now we're realizing that there's a medical internet. You've got things connecting between your brain and your gut, your mouth, your sinuses, and all over the body. You've got this amazing flow. And that can be bad or that can be good.

Dr. Jill 30:17
It's so important. And I love that we talked about the sinuses, the mouth, and all their importance. Let's go back to the importance of sleep. First of all, it's the chicken or the egg. Is part of Alzheimer's [caused by the] impairment in sleep and the circadian rhythm? Or is it that impairment and a lack of proper sleep are leading to cognitive dysfunction?

Dr. Dale Bredesen 30:38
That's a good point. And this is where so much of biology, I think, wants things to be linear and simple. I remember years ago, two experts were fighting about whether it was bad for your brain to have too much cortisol or too little cortisol. Well, of course, both [are bad]. There's a sweet spot for all these things. So it's the same way with these things, where poor sleep begets more Alzheimer's, and Alzheimer's begets more poor sleep. So, unfortunately, these are feedbacks that are positive. I

think of these as prionic loops where something begets more of itself. And unfortunately, you see that again and again and again. And it's really the nature of the signaling pathways in your brain.

Dr. Dale Bredesen 31:22
We think a lot about homeostasis, but what we forget is that when you have a multi-goal outcome, as with blood clotting or learning, you're trying to go from one part to another. So you're basically having a molecular switch: Oh, okay, make this synapse stronger right now quickly, or make a blood clot because you're going to die if you don't do that. So what you have is a feed-forward. And unfortunately, just as you were indicating, the same thing happens. It's not really a chicken and egg [conundrum]; it's kind of both. So, unfortunately, you're right: Alzheimer's does interfere with sleep. On the other hand, poor sleep enhances your risk for Alzheimer's disease.

Dr. Dale Bredesen 32:00
And there's more and more on this. I worry a lot about people who have low SpO2. There was an interesting paper a few years ago where they showed that if you just look at the mean SpO2 for the night, it correlates very nicely with the size of your hippocampus and other nuclei within your brain. So if you're sleeping and your average SpO2 is down to 89 or 90 instead of where it should be, 96 or 97, you are hurting yourself. You're not giving yourself the best chance. So absolutely, you've got to make sure the person doesn't have upper airway resistance syndrome, pouring out the adrenaline. You want to make sure they don't have sleep apnea, [which is] so common and, unfortunately, so underdiagnosed and so treatable.

Dr. Jill 32:45
Yes. So let me be clear: A workup for sleep apnea is part of the cognition assessment. My other thought is that, as we try to treat this, a lot of the treatments, like hypnotics or antihistamines, have an effect on cognition. So if you were to give someone something to help them sleep, would you go with [something] more natural first? Where would you go with that? And what would you say to avoid if you are experiencing cognitive impairment?

Dr. Dale Bredesen 33:12
Yes, this is a really good point. And there are all sorts of things that can exacerbate this. So yes, you want to avoid things that change your sleep pattern. You absolutely

want to avoid antihistamines if you can. You want to avoid anticholinergics. You want to avoid, just as you said, the sedatives; you want to avoid the various benzodiazepines. These are all things that very clearly increase your risk for cognitive decline. So what you want to do is look at what's holding it back.

Dr. Dale Bredesen 33:41
By the way, as you well know, a lot of times it's low progesterone. Progesterone is helpful for your parasympathetic system and helps you sleep. So if possible, having a normal level of progesterone is very helpful. Melatonin—just as with nitric oxide, melatonin declines as we get a little older. It is a normal product. And you don't want to take tons of it, but having small amounts of melatonin [can be beneficial], [such as] half a milligram or one milligram, [which is] typical. Or, for some people, [something] like three milligrams. But that general order. And I recognize that some people use 100 milligrams for other reasons. It does have anti-tumor effects. It does have anti-COVID effects and things like that. That's something separate. But for sleep, small amounts.

Dr. Dale Bredesen 34:26
Things like L-theanine are relaxing. We just saw, in the last few days, people talking about lavender sheets and these various inhalants that actually improve normal cognition, which is great. And that's one of my arguments: What we do to prevent Alzheimer's also enhances normal cognition. So there's no need to wait until you're having problems. You're going to improve your normal cognition as well. There are so many ways to go after this—just good sleep hygiene.

Dr. Dale Bredesen 34:56
And I know I'm guilty of this myself: Working on emails late at night, working or writing something, and then boom, it's time to go to bed. No, that's not a good way to do it. Get your blue blockers on. You want to kind of fade. So I'd be interested in your approach. How do you get people to kind of fade into sleep so that they get optimal sleep?—because I do think that is so important. Especially at least an hour of deep sleep, at least an hour and a half of REM, and at least seven hours of total sleep.

Dr. Jill 35:25
Yes, gosh, I love talking about this because I love sleep. And I think that's one thing I

do well. I think routine is so key because our bodies get into these rhythms even subconsciously. I take an Epsom salt bath in the evening and actually heat up the body so it can cool down; there's a temperature association with good sleep. So I think the optimal temperature is below 68 degrees in your home for optimal sleep; I think even lower than that might be optimal for our bodies, according to a study. Somewhere in the 60s is the optimal [temperature]. But our body, if we take a hot shower or bath, actually tends to allow us to cool down afterward. It stimulates the thermal regulation system, having the body cool down.

Dr. Jill 36:01
Basically, in the morning, when we wake up, the cortisol rises when we get that bright light exposure. That will actually help you sleep at night. So within five minutes of waking up, I either go get sunshine, water my flowers, or—I have a bright light system—on the dark days of winter, I turn on that bright light because that bright light in our retina before our coffee actually stimulates the rise of cortisol, which of course helps. And then our body temperature goes up, telling us it's time for waking up.

Dr. Jill 36:26
Then at night, we want our body temperature to lower, and we want no blue lights. Like you said, all screens have blue lights. You can now get apps and things to convert that. You can get blue blockers where you wear them. And then I found my deep sleep is best between whenever I go to bed, 9, 10, or 11, and midnight or one [o'clock]. And my REM is always best from 2 a.m. to 6 a.m. So if I skimp on sleep either way, I will see it impinge on my deep early hours and my REM.

Dr. Jill 37:09
PEMF [is something] I really like for deep sleep. I try that low level, like the Schumann frequency of 7 or 8 Hz, and I feel like that's a really good thing. And I'd love to ask you, "What other things?" We talked about all these basics, which is where you start. But red light, PEMF, and some of these other electromagnetic frequencies and things—have you found any evidence-based usage of these with cognition? Or lasers? Or what are the top two, three, or four things that you think really have promise as far as modalities?

Dr. Dale Bredesen 37:23
Yes, it's a great point. I've been mainly interested in: What are the mechanisms? We're now, by the way, trying to adapt these for ALS and frontal temporal dementia. Can we use the same principles while understanding that each of these has its own unique biochemistry and genetics? So I think that the future for all of us is to be able to prevent and reverse all of these different neurodegenerative diseases. The earlier, the better. And part of what's come out is some form of stimulation. Now, what is best? I tend to like the red light because, actually, there's a lot of data on it and it actually has the appropriate wavelength, for example, for cytochrome c stimulation. So I like that approach.

Dr. Dale Bredesen 38:10
Interestingly, as you know, 40 Hz has come back again and again and again in all the studies as being for some reason... whether it's 40 Hz sound, 40 Hz light stimulation, or whatever it is. Then, of course, Mert. Dr. Jerellyn Brossfield has done a really nice job looking at Mert with her patients—a magnetic form of stimulation. There's, of course, microcurrent. There are now [some] sound experiments. I tend to like photobiomodulation just because there is more data, I think, on it right now than others. But all of these represent some form of stimulation. And again, if you're going to work out with weights, you better have good nutrition. So you want to have all the other things working and then have this mild stimulation. You don't want to overdo it because you don't want to crash the system. But appropriate stimulation does seem to be very helpful, time after time.

Dr. Jill 39:06
I love how you frame that because I think it is so important. People get all these bells and whistles and expensive devices, and companies are trying to sell [them to] us. Even as physicians, they're trying to get us to buy the next $20,000 device for our patients. And those things can be helpful, yes, but it absolutely has to start with the foundational step that we first talked about. So this would be a good time to talk about diet. We haven't talked about diet yet. I know you have an incredible new program that you're releasing soon. I want to hear about that; I want you to share. But tell us about diet first, as far as: What are people looking for if they have cognitive impairment? Where do you start with diet?

Dr. Dale Bredesen 39:41
It's such a good point. I am not a nutritionist, so I'm sure I know far less about this

than most people listening. I'm simply interested in: What is the neurochemistry that makes your synapses function?—because this is a loss of functional synapses, when you are developing cognitive decline. So it turns out that you have to have all the things we've been talking about. You have to have the appropriate energetics. You have to have the appropriate trophic factors.

Dr. Dale Bredesen 40:07
I was really surprised to see beautiful work coming out of Emory looking at the biology of BDNF versus the biology of APP. These things are just intimately related. They have similar proteases that are involved with these things. It's amazing! So this is part of your normal neuroplastic chemistry. All of these things work together when you're actually trying to make people do better.

Dr. Dale Bredesen 40:37
So the common thing, as you know, [is that] people will say: "Okay, Dr. Jill, this is great, but it's just too complicated. It's hard for me. I don't know where to go. I don't know what to buy." This is why we put out the second book to try to be more specific, but then people said, "It's too much." So one of the most common things is, "Can you just give me something that does the right thing to help me out?" And yes, you have to hit several things. You have to hit the ability to be metabolically flexible. So you've got to be able to make glucose and ketones. You've got to get that plant-rich, mildly ketogenic, high-fiber good microbiome, heal the gut, and all these things. Heal the gut and heal the blood-brain barrier; these are all coming together.

Dr. Dale Bredesen 41:25
There are lots of ways that people have done this, but what has worked best is a plant-rich, mildly ketogenic diet with appropriate periods of fasting. Now, you have to be careful. People are often frail. You don't want to fast them too long, but you don't want to have no fast either. You want to have some time for autophagy. You want to have some time for the appropriate cleansing of the brain with your lymphatics. You want to do all these things that are appropriate.

Dr. Dale Bredesen 41:52
Actually, Julie G., who is an ApoE4/4 patient who's done very, very well for over 10 years now and has been a real activist and citizen scientist, and my wife, Dr. Aida Lashine, got together and worked with Nutrition for Longevity. This is the company founded by Dr. Walter Longo and Jennifer Maynard. [They] spent months and

months and months getting [to the bottom of], "Okay, how can you deliver to people and make it really easy?" Boom, you bring in meals. It's typically for Monday through Friday. "And how can you do that to make it really easy and to make it appropriately organic, appropriately pasture-[raised], appropriately wild-caught fish, and all the things that make it so that you hit all the right places for your synapses? So they now have this, and it's under KetoFlex. So you just look at KetoFlex123.com because it's a KetoFlex 12/3 approach.

Dr. Dale Bredesen 42:53
As you know, there are other diets that people have used, but they don't hit some of the biochemical parameters. They don't get you into ketosis at the appropriate time. Some of them don't have enough of the appropriate nutrients. So this is the one that actually biochemically works the best for cognition. And there are many people who have been using it who are living proof. I'd start with Julie, who's been doing this sort of thing for many, many years. So yes, please check it out. I've eaten them myself, and they definitely improved my ketosis. They are definitely very, very helpful. And I give credit to Nutrition for Longevity for making them delicious.

Dr. Jill 43:32
Oh, this is amazing because it's one of the most practical things that people, even my patients, who maybe aren't cognitively impaired, have trouble with. What do we eat? How do we eat well? And I think it's more and more complex. And what I love about the program—and I've been a fan of this for almost a decade now, [although] I don't know how long it's been—the plants are so crucial. And sometimes you hear 'keto', and people are just eating bacon and butter. And it's like, "Wait, no, no, no," right? And you and I totally agree on this. But I think that's so crucial for people to know that you can be ketogenic, or mildly ketogenic, as you put it, and still have a plant-based diet. And there's this really, really important place where they meet. I really feel like this is a foundation if you've had cancer—of course, the cognition. But this place where you're getting fibrous, nutrient-dense foods but also metabolic flexibility is really where we're landing for not only cognition but many other diseases.

Dr. Dale Bredesen 44:25
Absolutely. We were talking about the nature of the native immune system and where the memory is. So what happens is that you can become hyperactive. Interestingly, and it fits beautifully with this, if you eat saturated fats, you go up like

this. So now you are in a more pro-inflammatory state. On the other hand, if you're eating omega-3s, you're coming down. Interestingly, if you have [a history of] adverse childhood experiences, you're going back up. So anything that's causing stress is resetting that system to this more pro-inflammatory state. We discovered in the lab and published almost a decade ago that ApoE4 does that itself. So you've got to essentially counter that with appropriate things like omega-3s, curcumin, and things like that. And speaking of curcumin, I should ask you: Have you seen this stuff recently about curcumin being adulterated with lead chromate because of the yellow color?

Dr. Jill 45:18
Oh, I have. Yes. Yes, which is scary. Some of these things are like, "Oh, goodness!" Even kale and these wonderful leafy greens are used to pull thallium from the soil. So now some of these green juices, if you're not careful for a source, and they can be organic, have loads of cadmium and thallium. You're right; it really is scary.

Dr. Jill 45:40
Last little thing before I let you go. ApoE4—this is a big fear for people who have it or know they have it. Maybe if you're listening out there, you don't even know. What's the prognosis for ApoE4/4s? And basically, tell us what it is. And then what would you do differently for them? And what would their risk be for cognitive decline?

Dr. Dale Bredesen 45:58
Yes, great point. Things are changing dramatically because you can now check someone's p-tau181. Everyone should know that. You can check their Aβ40/Aβ42 ratio and, soon, their GFAP. So here's the thing: If you have no copies of ApoE4—and that's three-quarters of the population, most being [ApoE]3/3s, some [ApoE]2/3s—your lifetime risk for Alzheimer's is about 9%. It's not zero, but it's not too high. If you have a single copy—and that's 75 million Americans, and everybody should know it—your risk is 30%. Please get on some prevention. You don't have to get this. The biggest message for today is that Alzheimer's is now optional. Nobody needs to get this problem. So that's 75 million Americans. Please find out. Please get on active prevention. There are lots of great things to do. If you have two copies—that's about 7 million Americans, [and] unfortunately, the vast majority don't know it—your risk is up more like 70%. Most likely, you will develop Alzheimer's disease. So again, you don't have to. Please get on active prevention.

Dr. Dale Bredesen 47:01
Now, what does that mean? That means: Get a cognoscopy, and get on a personalized part. As Dr. Jill mentioned earlier, this is all about personalized medicine. That is the future, and that's the present now as well. But yes, you start with the basics, [such as] diet, exercise, sleep, stress, and all the things we've been talking about. And most people are going to do just fine with that. But find out. If you have a chronic infection that's undiagnosed, you can get it treated. Again, Lyme disease is such a common issue. So many people have it and don't realize it. Of course, long COVID is now emerging as a big issue for people's cognition in the future. Find out if you have exposure in your home to mycotoxins. Find out. Even if you're not having symptoms yet, you are at risk for them down the road.

Dr. Dale Bredesen 47:46
Get on an appropriate diet. Do a week or two of KetoFlex 12/3 through Nutrition for Longevity or one of these groups. It's a good idea. Get yourself in an optimal state. Performance is closely related to risk. So you get yourself in an optimal state, do these sorts of things, and you can lower your risk dramatically. I asked all the doctors I talked to, "Have you ever seen anyone who started when they were asymptomatic, did the right things for prevention, and still developed dementia?" I haven't seen one yet. I haven't heard of one yet. There will be some down the road. But at least what you can say is that it's very uncommon.

Dr. Jill 48:31
Tremendous! Thank you for the tireless efforts and work that you bring to the world, Dr. Bredesen. You are just a gift to humanity and a gift to so many, including myself as a fellow doctor who looks to you for guidance, wisdom, and research. We are so grateful—both the patients and the doctors. Let's just leave everybody with where they can find you and repeat the KetoFlex [12/3] and then your own Recode. Where can people find more information about this?

Dr. Dale Bredesen 48:56
Yes, thank you so much. I really appreciate that. And thank you, Dr. Jill, for all the great stuff you've been doing. And of course, I'm always hearing about wonderful, wonderful patient stories of people who've come to you and had such dramatic improvements. So thank you for all your great work over the years and, of course, your education and teaching for all of us.

Dr. Dale Bredesen 49:14
So where people can find [me is on] Facebook, Dr. Dale Bredesen. Also on Twitter, and also on Instagram. And then please be aware of the new randomized controlled trial. You can see the Evanthea Dementia Reversal Trial. That actually came from the mother of the donor who supported this work. She is very, very kind to support the doctors—Diana Merriam. We're grateful to her. So please, please check it out, especially if you're in one of those six areas that I mentioned before. Please take a look at this. And again, get a cognoscopy. You can look at mycognoscopy.com. You can also look at ketoflex123.com for meal deliveries. [They're] easy, delicious, and great stuff to have.

Dr. Jill 50:09
Perfect. And wherever you're listening, I am putting these websites in. You'll be able to see them and link to them. So if you didn't get that down, just come back to the landing page. We'll put all the links in. Dr. Bredesen, thank you so much! I'm so appreciative of all your work.

Dr. Dale Bredesen 50:23
Thank you, Dr. Jill. It was great talking to you, as always!

Dr. Jill 50:25
To you too.