Announcer: Bulletproof Radio, a state of high performance.

Dave: You're listening to Bulletproof Radio with Dave Asprey. Today's cool fact of the day is that mental cues can alter your physiology. A psychologist named Robert Ader, from the Rochester School of Medicine, this is a famous guy who coined the term psychoneuroimmunology, which was very ground-breaking. Anyway, he and his colleague, Nicholas Cohen, did this experiments in the 1970s. They trained lab rats to associate a stimuli with an event, like Pavlov trained dogs to drool when they heard a bell. But what these guys did is they gave rats an immune suppressing drug that had sweet tasting saccharine in it. Eventually the rats got so conditioned to the effects of the drug, that if they ate just saccharin without the drug, their immune system would also be suppressed.

Years later this was repeated in college students, believe it or not, and the same effect is true in humans. Which means you can have a quote "placebo" effect at the cellular level, even though the college students did not know that they were given an immune suppressant drug at all. They just knew, "Drink this weird tasking smoothie and come and do it again in a month." Pretty remarkable effect that there's stuff going on in our bodies that we don't know about.

Speaking of things that we don't know are going on in our bodies, today is going to be a fantastic, fantastic discussion with one of the guys pioneering Alzheimer's disease, and neurodegenerative diseases in our brains. You're gonna learn a lot. Even if you don't have Alzheimer's, you don't know anyone with Alzheimer's, you have a great chance of getting Alzheimer's disease, way more than you think. Assuming that you don't get hit by a car when you're young.

It's entirely, well entirely is going a little too far, it is exceptionally preventable if you understand the thing we're going to share with you today. So this is how to take care of your brain for your entire life, and stuff that no one knew about Alzheimer's.

Today's guest is Dr. Dale Bredesen. He is an internationally recognized expert in how Alzheimer's happens, and the Bredesen Laboratory studies the basic mechanisms behind neurodegeneration. Even if you're 20, you've already started a little bit neurodegeneration is called aging, and the deal is you could down a very bad path, or a dark path, or you could just have aging, or maybe even not much aging at all.

The things that you learn in the podcast today, and Dale's work, or Dr. Bredesen, has led to the publication of 220 research papers, and he just wrote an entire booked called, The End of Alzheimer's, that frankly blew my mind.

So Dr. Bredesen, welcome to the show.

Dale: Thanks Dave, great to be here.

Dave: We recorded our show on the deck of Dr. David Perlmutter's boat recently, with Dr. Jeff Bland. David Perlmutter and Jeff Bland have been guests on this show, so this was sort

of the superheroes of anti-aging and brain science, all on one boat. Then my memory card failed, so I'm recording another interview with you, which gives me a chance to pick your brain even more, and this is one we're gonna be publishing. So thanks for the extra time.

Dale: Yeah, thank you Dave.

Dave: Tell me about Alzheimer's. What is it that you've figured out that wasn't in the conversation about Alzheimer's 10 years ago.

Dale: Yeah, there are several pieces to this. One of the major ones is that people have tried to study this by looking at very tiny sets. Obviously you have a tremendous computer background, so if you went to an engineer and said, "Here's an incredibly complex organism, I've got 3.3 billion base payers, as the simplest part you've got tens of thousands of proteins with all sorts of modifications. Now something is going awry, and I want to figure out how to fix it. But I'm only gonna give you serum sodium, serum potassium, and a couple of other inputs." The engineer would laugh at you. This is much too big of a problem. But this is exactly what happens.

Dave: You're talking about looking at smoke to figure out what words were written on the page that was burnt to make the smoke, basically.

Dale: Exactly.

Dave: Okay.

Dale: We are getting much, much too small datasets when we look at people who have cognitive decline. And, by the way, this relates, as you alluded to earlier, to normal cognition. So a lot of people, in fact, could do better with their cognition by following these same sorts of approaches. So what we did was to look at the fundamental nature of the neurodegenerative process, and ask, "What is actually driving the biochemistry that leads of Alzheimer's disease?" People right now come into the doctor and they say, "I'm having trouble my memory, I'm having trouble with planning, what have you." The doctors says, "Oh yeah, that's Alzheimer's disease, and we're not gonna look at what caused it because we're gonna tell you we don't know what caused it." This is like taking your car and the mechanic says, "Oh Dave, this is car not working syndrome, we know all about it. It happens in older cars," and you say, "Well aren't you gonna evaluate some of the basics?" And the guy says, "No, because those tests are reimbursed." That is how bad things are today.

So when you look at larger data sets, and we currently look at 150 different variables in humans, which is a tiny number, actually, but it's far more than what others are looking at. What we found then, in 30 years of research, is there are sub-types of Alzheimer's disease, so you can see type one, two, three, et cetera, and also that this is a disease that is actually a protective responses of your brain to different insults. If you look at what's actually causing the problem, then you can address that, and we've had unprecedented improvements in people, and we published the first paper back in 2014,

another one in 2016, and we've got over two thousand people on the protocol now, and unprecedented improvements in people's cognition, with documental Alzheimer's, or pre-Alzheimer's, MCI, which is mild cognitive impairment, or SCI, which is subjective cognitive impairment.

If you actually look at what's causing the problem, you can get much better results

Dave: Do you see people in their 20s with SCI, subjective cognitive impairment? Or is this something that happens after 50?

Dale: Very interesting you should say that, because people will definitely get to an Alzheimer's diagnosis, which is typically about 20 years after you start the underlying patho-physiological process. And we certainly see it in people diagnosis of Alzheimer's, in their late 40s. So for those people, yes, it probably did start in their 20s. We have also had people begin to complain about what ultimately ends up as Alzheimer's, even in their late 20s. But, as you know, in general people start noticing the symptoms in their 40s and 50s, so that we have people ... And it's often around menopause, or andropause that people will begin to notice changes.

So yes, it can be in your 20s. We recommend that everybody who is 45 or over, get quote "cognoscopy", just as you get a colonoscopy when you're 50, you should get a cognoscopy when you're 45, and you may consider pushing that back to late 30s, because you want to know where you stand. And you want to know what is the biochemistry? What is your status? What is your risk? Just as you would want to know your cholesterol, or your LDL particle number, things like that, for your heart, you'd also want to know where you stand with a set of biochemical, genetic, and cognitive parameters, which are relatively easy to test.

Dave: What is in a cognoscopy? What are those parameters?

Dale: So when you go back to what's actually driving the decline, it is related to anything that produces inflammation, so chronic inflammation, whether it's from Borrelia, whether it's from HSV, whether it's from P. Gingivalis, or other organisms, or it's from leaky gut, or a poor diet, on and on. These things, anything that produces inflammation. We want to know Dave your hsCRP, you probably know your hsCRP. As you know, it should be less that one point zero.

Dave: That's High Sensitivity C-Reactive Protein. It's a common marker in inflammation panel, but only in advanced cardiac panels are you likely to see this if you go to a normal doctor. It's one of the big three things in Bulletproof that I tell you that you have to know, and it needs to be bullet one.

Dale: Exactly.

Dave: This is just for people listening so they understand that that is. And these other things you talked about, Borrelia, we're talking about Lyme Disease and associated factors.

HSV is a common virus that people get and, of course, leaky gut most people have heard of.

But these are things you wouldn't know about that are causing inflammation that are gonna hit your brain 40 years from now, but you know they're happening now.

Dale: Exactly. Then you want to know, and I usually ask people, "How many people here would like to avoid Alzheimer's?" And of course everybody's hand goes up. And then I say, "Okay, how many people know their hsCRP?" Probably 5% of people know their hsCRP. "How many people here know their Vitamin D levels?" And it's probably about 10%. "How many people know their ApoE status? Do you have a copy of ApoE four, zero, one, or two?" If you have zero copies of ApoE four, then you have about a nine percent chance, during your lifetime, to develop Alzheimer's. If you have a single copy, it's about a 30% chance. And if you have two copies, it's over 50%, so most likely you will develop Alzheimer's during your lifetime.

These are all things you'd like to know. You'd also like to know your fasting insulin level, because if your fasting insulin level is high, you are developing insulin resistance, which is an important risk factor for Alzheimer's disease and cognitive decline.

You'd also like to know your hemoglobin A1C of course, and then you'd also like to know whether you are exposed to specific toxins. These are metallo toxins like Mercury, organic toxins like DDE, for example, and of course, mycotoxins that you've talked about, and studied extensively.

Dave: They're molds.

Dale: There you go. Yup, mold. So here's the big surprise. When we wrote a paper back in 2015 showing that, in fact, many of these people ended up having exposure to mycotoxins. Who knew that mold was going to cause Alzheimer's disease? But for a sub-set of people, it absolutely does. And when you address that, you can get improvements in people. And if you don't address it, you're not going to get improvements.

So we call the inflammatory one, type one Alzheimer's, or hot, or inflammatory. Then the glycotoxic one is type one point five, because it actually gives you both the inflammation and the atrophic side, because you have insulin resistance. Type two is atrophic. You don't have enough support for your neural network, whether it's because of vitamin D, B-12, testosterone, estradiol, progesterone, pregnenolone, free thyroid, 3T3, on and on, and on. You need all these things to sustain your neural network, and if you do not have these, you end up downsizing your neural network. So that is type two atrophic, or cold Alzheimer's disease.

And then type three is toxic. This is often presenting in a very different way. These people actually look different, and you need to treat them differently if you're gonna rid of their toxin exposure.

Dave: Do you know how epic that one minute monologue was for everyone listening to this? You just summarized The End of Alzheimer's, your book, or at least the main points in it.

But here's the thing, we went from, "Your brain's not working, here's a retirement home, and you're not gonna remember your kids names," to saying, "You basically have one of these three things. There's an energy problem, there's a toxin problem, there's an inflammation problem, and sometimes there's overlapping." All of those hackable to one extent or another. Or, to put it doctor terms, curable.

How easy is it to prevent these versus reverse them?

Dale: Yeah. The reality is it's easy to prevent them. Easier, certainly, than reversing. And the reality is that Alzheimer's disease should be a rare disease. This is a trillion dollar global problem. Over 260 billion dollars was spent last year by the United States in Alzheimer-related things, nursing homes, drugs, so forth, and so on, lost wages. As you know, the caretakers for Alzheimer's patients also develop diseases, typically diseases associated with stress. They have shorter telomeres than controls, so this is a huge problem.

And, in fact, nobody should, or very, very few people should develop this problem. This is why we recommend that people get a cognoscopy. You can actually go on a website now, AHNPHealth.com, you can get a direct-to-consumer set of tests that will look at what your risk factors are. It will sub-type you and say, "Okay, you are most at risk for type two or type one point five, et cetera, and give you an initial program so that you can actually prevent the disease.

We haven't had anyone yet who's on prevention, who has developed cognitive decline. Now, we'll see. It's early days. But people who are on reversal, the most important thing here is that they sustain their improvement, unlike with drug treatment. The idea of going after a complex chronic illness like Alzheimer's, with a mono therapy, actually makes no biological sense. As we tell the patients, "Imagine you have a roof with 36 holes in it," 'cause initially we identified 36 different mechanisms that all contributed. And, by the way, everyone we've seen so far with cognitive decline, has between 10 and 25 different contributors. We haven't seen a single person yet, who has only one contributor to their cognitive decline.

So you want to identify these contributors, and then you want to address them. And as you said, the good news is, these are hackable so you, in fact, can address all of the contributors. The most difficult ones are, in fact, the toxins. When you've got someone exposed to mycotoxins you literally need to get them out of the house that is exposing them, or the building that is exposing them. And you need to detoxify them with things like cholestyramine, and then build things back with things like intranasal BIP.

But the good news is, all of these things can indeed be addressed.

Dave: I'm hoping right now there are a substantial number of listeners saying, "Oh my God I need to get this for my parents, or my spouse," because these tests aren't terribly expensive. I don't know how much AHNP charges for them, but these are relatively

common tests, at least most of them. If you want an advanced metals test, or a mycotoxin in blood or urine, they can be a little expensive, in the range of a few hundred dollars, but not a few thousand dollars.

Dale: Right.

Dave: And then, all of a sudden you go from, "Well, I have the symptoms and it's inevitable," to, "Well now I know something and I can make changes." How many of those holes do you need to patch, those holes in the roof, in order to reduce your risk to the point it's just unlikely? Do you have to perfectly fix all 36 of them, or just getting eight or twelve gonna get you so far along that you're gonna be happy with your life?

Dale: Actually, that's a really good point. To go back for one moment to the cost. It costs you about 120 thousand dollars per years to be in a nursing home, so you're talking about far less than one percent to do these tests. So yeah, it's a very good investment, in fact, to keep your faculties as you know.

Then, as far as the tests. What happens is very similar tow hat has been seen in cardiovascular disease. As you know, with cardiovascular disease what Dean Ornish found 30 years ago, is that once you get over a threshold, it's a little bit like a snowball rolling downhill. You're either going down the right side, or the wrong side. And what we've found is that there is a synaptoblastic to synaptoclastic ratio. In other words, there's a whole set of signals that is causing you to form new memories, and keep your memories. We call those synaptoblastic. And, on the other hand, there is an antagonistic set, synaptoclastic, that are involved in reorganizing memories, and you're doing this all the time.

When you're young those are in balance. As you get older, if you're low on these various supports, or if you've got exposure, you got inflammation, all the things we talked about, your synaptoclastic signaling outstrips your synaptoblastic signaling. So the good news is, the feedback here is actually antihomeostatic, so in biological systems when you have a single goal outcome, and you don't require signal amplification, you use, as you know, homeostatic feedback. That's negative feedback, like your serum pH. You know your serum pH? You want it to be seven point four, you never want it to be ten or two, so if you have an exposure to some acid, you know, you drink a soda or something, then your body uses metabolic and respiratory compensation to drive you back to seven point four.

However, when you have a system that requires signal amplification, and multi-goal outcome, such as forming synapsis, such as blood clotting, many other things. You actually have a feedback that enhances this, so it is a positive feedback. And, by the way, this is where preons come from. We call this preonic loop feedback. As you, for example, you cut your hand and you're gonna bleed to death if you don't make a clot in a certain amount of time, you have a system of searing proteases that feeds forward to develop that clot for you. And then, of course, over the next week or so, you begin to break that down.

Same thing happens here. The good news is, once you get over the hump, and the first patient we had, out of the 36 holes, she addressed 12. But, for her, that was enough. The problem is, we don't know ahead of time how many it's gonna be, so we keep adding them, because if we don't help the person they're gonna die of Alzheimer's. We continue to add until they get reversal. And this first person, 12. For people in prevention, it's often four or five, it's not a lot. For people, the farther the road they are, the more of these you have to address.

Dave: Do you have a stack ranked list for the average person that says, "This is the number one of 36 to go after," because it's such a low-hanging fruit, because it's so common, and this is number two. Could you tell us the top five things on your list?

Dale: Sure. So the way works though is that it's personalized. So your top five will be different from my top five, will be different from someone else's top five. We have a computer-based algorithm that was use, that goes through each thing, all the different possibilities, and then says, "Okay, look. Here's an example. Dave, if you have mycotoxin exposure, and you have HLADRDQ that is sensitive to mycotoxin exposure-"

Dave: That would be me.

Dale: There you go. So that would likely be your biggest hole in your roof. That's gonna be your number one priority. For many people, it will be a hormonal imbalance. So if you have a estradiol level that's very low, or if you have a testosterone level, or if your thyroid is very low, or you vitamin D is less than 20. These things could be very high on your list.

Dave: All of those were me in my 20s, but they're not me any more.

Dale: And there you go. So you addressed all of these, and probably averted some significant cognizant issues down the road. For many people, and you mentioned the top five. If you just take the group as a whole, and that can be dangerous of course because, for example, we have about five percent of people, Mercury is the critical number one. Until you address that, they won't get better.

But for the other 95% of people, Mercury is not a big issue. So no surprise, when you do these big population studies, you come away with the idea that mercury's not important. But for that five percent, Mercury is very important.

If you look at the population, here are the big five. Number one, glycotoxicity and insulin resistance. So most people have toxicity from sugar. We simply were not built, as you've pointed out many times, evolutionarily to handle the number, and the calories we get from simple carbs. We develop insulin resistance, we develop inflammation, and sometimes metabolic syndrome, due to the glycated proteins and our immune response to them. That's one of the big five.

Second one. Continued chronic inflammation due to typically different organisms, and we actually need to look for these organisms. And we're finding many people looking at

PCR from urine, for example, many people who end up having not simply Borrelia, and they've often been treated for Lyme, but unfortunately they have a co-infection. They have Babesia, or they have Bartonella, or they have Ehrlichia, or Anaplasma and, until you address those things, they're not going to get rid of that chronic inflammation.

Dave: With Lyme Disease, or Borrelia, somewhere around 95% of people have some Lyme spirochetes present, if you measure their urine, but they don't have any active Lyme Disease. It's been my experience from talking with a lot of people, that most people don't get chronic Lyme until they're exposed to another toxin. Usually mold toxins but sometimes Mercury, but something takes out the immune system, and then the Lyme grows, and then they get chronic inflammation where they're screwed. I mean, do all of us need to worry about Lyme, in the context of Alzheimer's or not?

Dale: This is a great point, and it brings up the fact that what is Alzheimer's? As I was mentioning earlier, this is really a protective response to different insults. What happens is, the amyloid that has been vilified in Alzheimer's, where the companies are telling you, "We've got to get rid of that amyloid," is very much like napalm. Imagine you've got invaders breaching your borders, so you're gonna put napalm down around the borders to try and kill the invaders. This is what your brain is doing with amyloid. It's putting down the amyloid because it is an anti-microbial, as shown very nicely by Professors Robert Moir, and Rudy Tanzi from Harvard, a number of years ago. You're putting this stuff down, but now you're living in a smaller, less arable soil, smaller country. You are literally downsizing.

Yes, what we call Alzheimer's is a chronic activation of the innate immune system, and amyloid beta is part of the innate immune system's response. So as you indicated, as long as you can keep the Borrelia at bay without your amyloid, you're in better shape. But as you now start to fail to do that, you've got to put down that napalm, that amyloid, and as long as you are fighting these various agents with amyloid, you are now downsizing, you are now at risk for Alzheimer's disease. And you may end up at the SCI stage. You may end up at the mild cognitive impairment stage, or you may end up going all the way to Alzheimer's. But that's why you need to address these things.

And yes, there are many of them that can do this. As an example, we had one patient who did very well, and had the Borrelia treated years before, but was continuing to have incomplete recovery, and ultimately we found out she had babesiosis, which is essentially a relative of malaria. It's a parasite. And as she's now been treated for her babesiosis, she's got continued improvement.

So the answer is that yes, you have to be concerned about these things. And as you pointed out, so many of us have been exposed to these. Now, one way to deal with them is simply enhancing our own immune system function, and that is through good diet, all the things that we do. Sleep, lowering stress, exercise, and some people like to use the old approach that the Ayurvedics use, which is this triad of [amelachie 00:26:34], Ashwagandha, and [tenespora 00:26:34]. A very good way to support your immune system function.

So again, there's a whole set of things. This is a concert. You've got to get everything right to get this. And now, if you fail in these, then ultimately yes, you've got to be concerned that you will have the Borrelia essentially loose, and that you've now got to use amyloid and that you are at risk for Alzheimer's disease.

Dave: Is there a case for maybe taking one month every year and just saying, "All right, I'm gonna take a broad spectrum of anti-parasitics, I'm gonna the Ayurvedic trifecta you talked about there, I'm gonna take Mercury, [inaudible 00:27:17], and I'm basically gonna go through ... Because I don't know what I'm exposed to on a daily basis. Nobody does.

Dale: Right.

Dave: And just going through and just cleansing the crap out of yourself, for lack of a better word, as a preventative approach. Or is this something that needs to be more nuanced on a regular basis? Because most people listening aren't going to go out and get the test, and most of them are gonna do a few different things when they realize how much power, and how much likelihood they have of getting Alzheimer's.

A shout out to Maria Shriver who talked about all those statistics, how women get it quite a lot as well as men, and et cetera. But is this something that could work for people? See, I don't really know which of these I have, I'm just gonna get the big ones, and just do it on a regular basis until I'm 120.

Dale: It's a great point, and I think there are two ways to go about this. One of the things we're doing actually, is making this easier, and easier, and easier, because again, the reality is this should be something of our everyday lives, this should be something where nobody gets this, or very, very few people ever get this disease. You're right. We need to know things like our fasting insulting, homocysteine is another good one. What's your status of methylation? I do think this will become part of our lexicon, this will become part of our everyday lives, this will be part of the zeitgeist, just as pretty much everybody knows what their cholesterol is, most people know what their blood pressure is. You could have said 50 years ago, "Hey, who's gonna go out and get a blood pressure cuff and actually check themselves?" "Hey, who's gonna go and actually prick their finger and see what their glucose or their ketone level is?"

I think that when you realize that this will not only make a difference in whether you will develop a terminal illness or not, imagine if you could do the same thing Dave, to tell you, "Dave, you're never gonna get cancer. Don't worry about it. You're never gonna get cancer." It would be something that would be, "Hey, is something I maybe want to check every now and then." So we want to make it easier and easier, but you're right, for today, maybe people will simply say, "Well, I want to do some things right."

And yes, you've already talked about so many of these. What we call the Ketoflex 12/3 diet, which I talked about in the book, low carbs, driving yourself into mild ketosis, having specific periods of fasting, you want to optimize your microbiome, there are some definitely some things you can do, exercise, reduce your stress, meditation, sleep.

Sleep is a huge issue. Make sure you don't have sleep apnea, that's an important contributor for many, many people. Do some brain training. There are some specific herbs and supplements you can take. All these sorts of things, obviously probiotics, prebiotics, make sure to heal your gut.

So you can treat blind. I don't recommend treating blind, because there are so many things that can impact you, but I think as it becomes easier and easier that you can take a few hours and get checked out, I think that many, many people will realize that can literally save my life. This is where we're headed for all complex, chronic illnesses. I'm working with people now also with macular degeneration, with Parkinson's, with Lewy Body, these things are all things that can be prevented.

Chronic illness medicine and health is completely different than 20th century medicine. You need to address it differently.

Dave: Dale, I feel like if people were to apply your Alzheimer's protocols and just say, "Well, what would happen with macular degeneration?" They would see similar things. And a lot of the research that I drew on to write Head Strong, I look at Alzheimer's research, including yours, and I looked at Parkinson's, because these are the worst case in scenarios, and I focused very specifically on energy production, which I think would be more type three in your thing, but relevant to all of them.

But the idea is, if you reduce your odds of one chronic disease, you're probably going to reduce your odds of all chronic diseases, at least some. Do you agree with that mindset?

Dale: So here's the interesting thing. There's a Venn diagram, obviously, where you've got a core that is absolutely similar. You're right, so many of these illnesses are related to our microbiome, our leaky gut, our use of high simple carbs. The bottom line is, we are, by the way we are living, giving ourselves these diseases and our doctors are not recognizing that, and they're telling us, "You've got some disease. We don't know why you get it. Let me give you a drug that doesn't work very well." This is a very old-fashioned way to deal with these things. You're absolutely right.

However, the Venn diagram does not have a perfect concordance, and here's an example. You are at increased risk for macular degeneration if you're ApoE 4 negative, and you're at increased risk for Alzheimer's if you're ApoE 4 positive. So there are definite differences. But the good news is, there's a lot of basic research that now points us to the pathophysiology of each one of these. So you can see, essentially, what I would call ... So my argument is, these are what I would call mismatched diseases, so this is the mismatched theory of neurodegeneration that I'm suggesting, where any time you've got a chronic or repeated mismatch between supply and demand, you have a network downsizing. If the supply and demand is entropic support for the brain, where plasticity is an issue, you develop Alzheimer's. If it's for your macula, where there is as you know, a very, very high metabolic rate, and the demand there is because any time you're looking at blue light, if you're staying up late, if you've looking ... You've got more light exposure again than we were meant to support. If you've got specific genetics, things like the CFH gene, as you know. If you've got too low zinc, too low trophic factors. So now this same story, but in that system.

Same story if you now move it to mitochondrial complex one, you develop Parkinson's. And for each of these the downsizing program is designed to relieve the greatest amount of stress with the least loss. So in fact, this is why people walk around with the pathophysiology of Alzheimer's for 20 years. They still drive, they still play tennis, they still do their work, they start to have trouble memorizing new things. They being to lose that plasticity.

But you've got the same sort of thing for each of these diseases. You're right, there's a lot of core similarity, but there are also specifics for each one of these, and you can address them.

Dave: I'm looking at the speed of your work. You came out with Recode, your reversal of cognitive decline protocol in 2014-

Dale: Right.

Dave: ... and here we are four years later, and a lot of the tests that you use in that are widely available. You can order them at home, without even having to go to the doctor. And it seems like the speed of the knowledge for Alzheimer's is pretty good. I feel like the speed of our understanding of the many different factors that into the things that take us out, heart disease, cancer, diabetes, Alzheimer's, macular degeneration I actually put on that list as well. Those are the things that kill most people, if it's not falling rocks or something.

Dale: Right.

Dave: Do you feel like we're getting to the point in the next five years, ten years, where we're going to know enough that a person with the motivation, and reasonable means, can go out and say, "I'm gonna get tested every one or two years, understand where I am on all these things." So that we can avoid all of those deaths for those causes?

Dale: Absolutely. And you can do most of this now, as you know. I really do believe we are at an inflection point. As you know, we worked on this in the lab for 30 years, very slowly looking at cells dying, and mice, and making mice better with mouseheimer's. But we're now to the point where we can actually see human beings getting better. We can actually see what drives the neurodegenerative process. So yes, I certainly think just as you're hacking these various different biological parameters, we are now able to look at what's contributing to most of these illnesses for people. So yes, I think it will be more and more common for people to prevent, and especially early reversal, of all of these diseases.

Dave: What's next? So after we've gotten rid of these primary big causes of mortality, put on your future hat. You spend many, many years looking at Alzheimer's in brains, and you're a physician. What should I be worried about on my path to live until 180 after I've hacked all of these in my own biology?

Dale: Well you know, this is a really good point because the 20th century medicine was about what it is, and we were able to treat simple diseases, like pneumococcal pneumonia and TB. 21st century medicine, which is unfortunately not being practiced in the vast majority of practices today, is about why. So you're looking at all the disparate parameters, so there must be a much better interaction between Silicon Valley, and healthcare. That has failed so far. We've done things like electronic medical records but, in terms of applying very large data sets to these complex chronic illnesses, which is absolutely what's needed, this hasn't been done. Every doctor's office should have tremendous computing power, because they are dealing with human organisms that are incredibly complex.

Now, after that is done, we now can prevent Alzheimer's, prevent most of these chronic illnesses. The question is, if we've gotten rid of acute illnesses, and we've gotten rid of most of the chronic illnesses, we are actually now really left with the chronometer. We're left with the aging phenomenon. What's interesting is, the aging research right now is debased and adulterated, because there is so much of complex chronic illness, we're killing ourselves with these various things that we're doing wrong.

Once we optimize things for our evolution, now we really do peel back the onion and you really do see, "Ah, what is the underlying aging process?" Now the good news is, we can start addressing that. If the first thing that's going to get you is your telomeres, okay. You can address that. Is the first thing that's gonna get you, no it's actually be your DNA mutation. For example, mitochondrial mutations, as you know, if you look at what is the ratio from birth to death, the highest change, it is in mitochondrial DNA mutations. It's many orders of magnitude, as you know.

If it turns out to be misfolded proteins, so now we actually will be able to focus on aging research. Most of what we call aging today is, you sucked at living, right? Isn't that really what it is? You ate sugar, you went to the wrong doctor, you took medicines for everything, you sucked at living. And that's most of what we call aging right now. So when we-

Dave: That's my favorite quote, from all of Bulletproof Radio. Sorry, keep going.

Dale: But isn't that true? Most of us are not doing the right things, and that's what's killing us. The really cool future is, we've gotten rid of the infectious stuff, we now are onto the chronic illnesses and, by the way, that reveals all sorts of new infections, as you mentioned earlier. Borrelia is so fundamentally different the pneumococcal pneumonia, it really is the neuro-syphilis of the 21st century. So now we get rid of these pathogens, we get rid of these biofilms, we start to do the right things with our living, we optimize what we are doing evolutionarily, now we reveal what aging is really all about. Now you saw, "Hey Dave, you know what? Your telomeres are looking good, but you know what? You need some stem cells." Okay, you get your stem cells, and now you really do begin to see.

I always tell people we want to make it so that you can live happily and healthily until 100. But now you're gonna live to 120, 140, as you said, maybe 180. What is not the next limiting feature? And a lot of it is gonna be taken care of with things like stem cells,

appropriate folding of proteins, removing your senescent cells potentially. As you know, there's a big push to removing the senescent cells. So now you're actually gonna look at aging instead of simply chronic illness.

Dave: That is such a powerful summary. And the reason I asked you the question was a little bit self-serving, because I feel like I've got a good handle on my risk for these major killers, and I know that there are people who live to 120 today. All right, that's doable, and I'm gonna do everything to make that happen, and I'm counting on another 50% of my lifespan from new technology. But I'm not even sure what that new technology is going to be aimed at yet, but those things you just named are the top ones on my list as well. Is it telomeres? And I'm doing some stuff to lengthen my telomeres. But if we say that that's really important, and we start applying as much energy to lengthening telomeres as we do to, I'm just gonna say, useless heart disease research, that hasn't generated any benefits over the last 50 years. That sort of economics into it would change everything, and I want to make sure that I'm way ahead of the curve, because that whole not dying thing is part of my anti-aging strategy.

So I'm always looking to someone with your incredible knowledge of these things.

Dale: No question. Dying gets in the way of healthy aging, no question.

Dave: Yeah, step one, don't die. Everything else is a detail, right?

Dale: One of the things I was going to say, I'm really interested in how do we make it so that our children, and the teenagers, and the 20-somethings, plan their lives? I think strategic living is gonna be more and more common, and more and more important. Our own two daughters do many things that I didn't know to do when I was their age. And so they're eating the right things, they're doing the right things, they're checking the right blood values that I didn't now to check. And I think both strategic conception, getting a healthy baby, and strategic living, will be much more common with these generations.

Dave: My very first book was called The Better Baby book, and it's what we did for our own children to give them that head start, because you want to talk about leverage? It's three months before you get pregnant is when you have the best leverage, and you lose leverage with every minute of every day until you're 120. It always declines. It's just so easy to get one little variable right. Like fewer neurotoxins in the first trimester. If your Mom did that, even if her Mom did that, your odds of living a very long time go up dramatically. I have great hope, because I see what I did when I was 16, thinking that it was a good thing, or at least it wasn't harmful, and knowing now what a complete trainwreck that was.

I believe we've learned enough as a species that what are teenagers are doing now is more directionally accurate, because we all think it's right, but when I was a kid eating Coke, and beverages like that just full of sugar because, "Hey, it's just calories. As long as I don't have too many calories it doesn't matter." It was just wrong, but I thought it was right.

Dale: Absolutely.

Dave: Is there a chance that what we're telling people to do now is just fundamentally wrong, and we're gonna find out 50 years from now that are completely clueless?

Dale: Very interesting point. So, as you'll recall, Roy Walford years ago, was interested in living a very, very long time, and unfortunately ended up dying of ALS. One of the suggestions that's been made is that you can drive yourself too much and, in fact, put too much stress. So what happens is, you have different systems, each of which has a stress point. Therefore, you can drive yourself to less Alzheimer's, but you may end up with something else. And one of the arguments for ALS is that you have to clear glutamate from your synapses, you have to have a certain amount of energy to do that and to deal with this. So, in your efforts to try to drop your energy level and have greater longevity, you may end up hurting yourself because you actually have to have a certain amount of energy to deal with every day living.

I think the key is gonna be that, although we all agree that many of these approaches are helpful, we were not made to have insulin resistance, so forth and so on. But you're absolutely right. If we're not careful, we can expose other problems. I'll tell you one we've run into with the treatment of cognitive decline. We get people on, we drive them into mild ketosis, from 1.5 mm to 4 mm beta-Hydroxybutyrate. We're getting rid of their insulin resistance, reestablishing insulin sensitivity, addressing their pathogens, addressing detox, all these things. But what we found is that the people who have BMIs, typically below 20, as they're now decreasing their carbs, they don't have the adipose tissue to produce the ketones that are supporting their cognition.

What happens, they're the ones that actually have problems at the beginning. And so we now often add exogenous ketones, or more MCT oil, things like that, to make sure that they actually check them. We've had a few that will actually develop gut problems, lose weight, and actually take a step back in the cognitive decline before we address the fact that, "Oh yeah, you guys are not able at this point to generate those endogenous ketones, so we in fact need to help you and get your weight up, liberalize your diet, cycle in and out of ketosis," all those sorts of things.

So as we learn more and more, we can tweak this, and make it better and better. But yes, you're right. These things are not black and white. You have to, for each person, customize this for his or her genetics, his or her biochemistry. We always talk about genotype and phenotype, but we also want to include the chemotype. Where do they stand with their biochemistry so that we can address all these appropriately?

Dave: You mentioned cyclical ketosis there, which is something that is a core part of Bulletproof. I look at people who are on higher carb diets, and they're in a state of relatively high glucose-

Dale: Right, right.

Dave: ... and it never changes. And when you get the idea that, "Okay, that's bad," it's very easy the way humans think, to say, "All right, I want to be in full-blown ketosis all the time, unrelenting, unending." And that also seems sort of the other side of the coin, of excessive high glucose with excessive high ketones. Whereas we might want to be able to metabolize carbs, so we go out of ketosis and back into ketosis, and usually have some ketones floating around because of MCTs, or because we fast on a regular basis.

Dale: Right.

Dave: Do you see long-term problems with having high ketone levels and just no carbs ever? Or is that gonna work for Alzheimer's and things?

Dale: So it so far would seem that having chronic ketosis seems to be a good thing for mentation, and seems to help you. However, as you know, over time you can develop essentially some resistance. You can lose the metabolic flexibility, the very metabolic flexibility you're trying to achieve. This is why, for many people, it is a good idea every once in a while. Whether you do it once every week, or once every two weeks, to cycle out of that briefly, to keep yourself metabolically flexible. That seems to work better.

Dave: That's something that I hope comes out. I know when I started talking about that, some of that all comes out, the keto-bros. You know, "All ketosis all the time. If you ever have a carb again you're in league with the devil." It doesn't seem to work like that biologically. Is there a role though, if someone is in the early stages of Alzheimer's, is there a role for them to have even moderate amounts of starch on somewhat of a basis, to support the glial cells in the brain that want glucose? Or, at that stage, when you're that far down, at the beginnings of Alzheimer's, to heck with glucose, it's all about ketones?

Dale: Well, so resistance starches, and some starchy vegetables, these things are very reasonable, and so we certainly include those. Again, you don't want to go crazy on sugar. But yes, things like resistance starches, and some starchy vegetables. So yes, we do need protein and, by the way, protein as you know, too much protein can also give you problems with insulin resistance. So we typically suggest one, typically 0.8 to 1.0 grams per kilogram of lean body mass. But, if you are detoxing, as you know, you need to go higher than that. So again, it depends on where you stand.

If you are a person with type three Alzheimer's, you need to increase the protein a little bit. So yeah, there's a role for all of those macronutrients, as well as many, many phytonutrients and micronutrients. But typically, you don't need sugar.

Dave: I could not agree more with you there. Although sugar is delicious, I must say.

Dale: Yeah, it's amazing how much of a drug it really is.

Dave: I mean, I hear people say, "I couldn't give up sugar," and I say, "You know? I know someone else who sounded like that, but their problem was heroin. I'm sure heroin's delicious, never tried it." But it's the same sort of thing. You just don't do that. And if

you get a couple of grams of sugar that was in our asparagus, it doesn't matter. But if you're putting teaspoons of it on there, it does matter. Since we Stevia, and have monk fruit, and we have xylitol, you can still have a sweet taste, you don't have to live life eating cardboard all the time, which doesn't work.

Dale: Exactly. And you've got berries and things like that.

Dave: Right. So I've got two more questions for you. There's a declining group of people who still say you need to be on a low fat diet if you don't want to get heart disease, and that you should get less than 10% of your calories from fat, and you should have lots of starchy carbs and things like that. How does that jive with your work?

Dale: It's a very interesting question and, of course, it's an ongoing controversy. We're going very simply by what makes your brain function better without hurting you. So, as you know, the brain needs fat. The patients we're dealing with are typically on diets that are 70% of the calories from good fats, and initially actually, as you know, some medium change triglycerides and things, so saturated, fatty acids as well. And then, at the time they go on, they check their LDL particle number, and you can literally adjust this. If you LDL particle number is too high, you can go down on the saturated fats, and you can go up on the monounsaturates and polyunsaturates. And if it's good, you can then balance those.

What we find is that these people do well. Low fat diets are associated with smaller brains, as you know, with some atrophy. And so we want to be careful about that. As an example, one of the people we're dealing with has ApoE 4-4, the very person who's not supposed to eat much fat. She eats 70% of her diet calories with good fats, has some protein, has no simple carbohydrates, and is doing extremely well. And, by the way, her lipid profile is outstanding, and her LDL particle number, less than a thousand. She looks great and has clean coronary arteries.

I think that the reality was it was something that people tried to get these lipid numbers down low, but it has not turned out to be good for your brain overall.

Dave: So we end up saying, "I'm gonna reduce my risk of heart attacks," which is also debatable, when you look at all the data. But you do that at the cost of your brain, it's not a good strategy. And I've been on diets like that when I was trying to lose the 100 pounds of fat I used to carry around, and you don't feel good on it. You might feel good for a little while, but then it's not a good thing.

I would like people listening to say, "Look, if you try to diet like that and your brain works, and you're losing weight, and your numbers look good, more power to you. That's awesome." It just doesn't seem to work for the vast majority of people. And the ones who do it, over time, the decline is apparent. And what we're looking to do is create this nutritional profile that says, "I'm not gonna get Alzheimer's disease, I'm not going to get cancer, I'm not going to get diabetes, and I'm not going to get heart disease." And to get all of those at the same time, it's going to be individualized, but the

general rules are, tons of vegetables, like you said, phytonutrients, not eating sugar. What about grains? I would say, don't eat grains, but where are you on that?

Dale: Yeah, it's a good point. The big four, we always talk about our simple carbs, grains, dairy, and lectins. Now, different people can handle different amounts of those, some people are more sensitive. And again, lectins we kind of go, "Last," because it depends if you are particularly sensitive to them, and if you have autoimmune problems, think about those. It's basically getting rid of nightshades and legumes.

But, as a general rule, grains, whole grains have been used, as you know, they do have a nice effect because of the fiber, et cetera, and they do have some protein and things. But they do have potential damage and so we generally suggest to people, until you know more, stay away from grains and really focus on the vegetables, the low-glycemic fruit. You want to have a very high, both soluble and insoluble fiber. It helps your biome, it helps your absorption of any sort of carbohydrates, it is great for detoxing, so these are very, very helpful. In general, we suggest people stay away from grains.

Dave: Me too. If someone came to your tomorrow Dale, and said, "I want to perform better at everything I do as a human being, and not just from a medical perspective, but just at life." What are your three most important pieces of advice, what would you offer them?

Dale: I would say, first of all, get a cognoscopy check. In other words, check out your biochemistry. If you happen to have methylation issues that maybe other people don't have, you can address those today. As you indicate, as you have said for years, these things are hackable. And, in fact, optimization is hackable. Step one is, get directions for what you need to hack based on your genetics, and based on your biochemistry.

The second thing, get direction based on your psychology. Many people will say, "Okay, I understand there's a program here that's gonna help me, but I just don't want to do it, or I don't like it." Some people need the carrot, some people need the stick. One of the guys I worked with, by the way, who had a tremendous increase in the hippocampal volume, did absolutely great, ApoE 4 positive, CAT scan proven Alzheimer's disease, he's done very well. He said, "I need a dominatrix," and I said, "You're talking to the wrong guy."

Dave: A food dominatrix, right?

Dale: Yeah, he needed somebody to say, "You've got to do this program." Because he was under a lot of stress, he would go home on Friday night after working very hard at his job, and get a couple of pints of ice cream and down them. Of course, that was hurting him. It turned out he had many, many different metabolic alterations that were all fixable, and when they were fixed, he did absolutely great. And he's doing great to this day. He's about three and a half years into this. So that would be number two. Get the right psychology for you.

And then number three I would say step back and have the joy that we should all have. We're all so worried about everything from politics to whether we achieved what we

wanted to achieve, that are we gonna die tomorrow? I think that having a positive attitude about these, and recognizing, "This stuff is doable," you know? As Steve Jobs said, "The people who are crazy enough to think that they're going to change the world, are the ones that actually end up doing it." So you can do it, each person. Optimize your biochemistry and given your genetics, optimize your psychology, and then step back and recognize that there's a tremendous amount of excitement to living, and that you can make the changes that other people are telling you you can't make.

Dave: Absolutely love that. One final question, we'll call it a bonus question. Coffee and Alzheimer's, good or bad?

Dale: Well, you know, it's really interesting you should mention that. The data are clear. People who drink coffee typically five cups or more per day, have a lower risk for Alzheimer's. Now, that's not to say it's the optimal thing to do necessarily. Be careful about your adrenals, as you know-

Dave: Yup.

Dale: ... and as you've point out, there can be stuff in some coffees that you want to avoid. But, in fact, people have tried for years to show that coffee's bad for you, they've never really been able to do it. And so the reality is, you increase the cyclic AMP. You can actually look back and see why, in the 1950s and 60s, people had coffee and a cigarette after lunch. You get the cyclic AMP up, you get that nicotinic acetylcholine receptor activated, you're gonna remember better, and you're gonna form new memories, and you're gonna function better.

We know now, you don't want to include the cigarette. But, the reality is, we're understanding more about these pathways and, in fact, increasing your cyclic AMP, whether you do it by coffee or other means, is good for you. We also recommend people increase their BDNF, and things like that. But we're understanding more and more, the pathways that are giving you better function and preventing decline. And coffee contributes to an important one.

Dave: It's funny you mention nicotine. I just did a interview with a professor from Vanderbilt, who published the first study in 1988 on oral nicotine, not smoking, but actually eating nicotine to treat Alzheimer's disease. So maybe those 1950s and 60s people with their coffee and cigarettes, smoking's nasty, maybe they were onto something here. In fact, while we're on that, I think I'll have one milligram of nicotine. There. Not I'm set for the day.

Dale: Very interesting.

Dave: All right Dale.

Dale: All right Dave.

Dave: I love your work. Everyone listening, it's drbredesen.com. His book is called, The End of Alzheimer's. You actually need to read this book. I don't use need, it's a weasel word normally, but seriously, if you want to join me on this living to 180 thing, there is groundbreaking info, it totally blew my mind. Absolutely worth your time.

Dale: Fantastic. Thank you so much Dave.

Dave: If you liked today's episode, you know what to do. Head on over to Amazon and pick up a copy of Dale's book and read it and, when you're done reading it, leave a review for him that says, "This book was worth my time," if you think it was, which it will be.

And since you're already on Amazon, you're already leaving reviews, tell someone about The Bulletproof Diet, or Head Strong, or Bulletproof Coffee. Just take a second to leave a few of those five star reviews, because people who make good stuff like Dale's book, we notice that stuff, and we're always thankful if you take the time to do it.

Have an awesome day.