Alzheimer’s: the third leading cause of death in the United States. What can you do to protect yourself from it? Hi, this is Dr. Mercola, helping you take control of your health. Today we have the privilege of being joined by Dr. Dale Bredesen, who is a physician, although if you look at his credentials, you’d think he was a physician, Doctor of Medicine and of Philosophy (MD-PhD). He graduated from Duke University. He’s now serving as the director of Neurodegenerative Disease Research at the University of California, Los Angeles (UCLA) School of Medicine.

Interestingly, he also went to California Institute of Technology (Caltech) and worked at Massachusetts Institute of Technology (MIT), two of the best engineering schools in the world, and has a profoundly deep and passionate interest in math, which is of course one of the most foundational basic sciences. He’s done some incredible research. He’s probably one of the most credible and leading researchers in Alzheimer’s who I’m aware of. I’m just so privileged to have him to discuss some of the research findings he’s come up with that can have an enormous impact on you. Welcome and thank you for joining us today.

DB: Thanks very much, Dr. Mercola. Great to be here.

JM: Alright. I guess we could start with the fact that Alzheimer’s is the third leading cause of death in the United States. Many people aren’t aware of that. It seems to be behind heart disease and cancer. Those may flip at some point in the future.

DB: Right.

JM: Just so that we can set the stage and then talk into the number of brilliant molecular mechanisms that you have been able to identify and programs you’ve put together to help treat it, I’m wondering if you could set the stage for your projections as to the impact that this disease process is going to have in the next generation or so.

DB: Right. You hear things that sound like hyperbole when it comes to Alzheimer’s disease, but unfortunately, they’re not. It’s currently costing the United States over 220 billion dollars annually. It is a trillion-dollar global health problem. As you indicated, it’s on the rise. It was the sixth leading cause of death, which is commonly quoted. Now, it has become the third leading cause of death in the United States. This is something that’s set to bankrupt Medicare. It strikes about 15 percent of the population, so incredibly common.

In fact, unfortunately, you have the pathophysiology of the disease for about 20 years before the diagnosis is made. Many of us are walking around with early Alzheimer’s without realizing.
[It's] a huge, huge problem on the rise, and there hasn’t been any sort of a monotherapeutic approach that has worked for this terrible illness.

**JM:** Some experts are projecting that it’s going to impact up to half of us in the next generation. I’m wondering if you would agree with this assessment or do you have different ideas as to what the impact is going to be? Unless something radically changes it, I don’t think it will.

**DB:** That’s a good point. It may well [be], because we know that if you simply look at the age-related incidence, then you’re looking at by the time you reach 85 – The prevalence increases. By the time you are reaching 85, nearly half of the people are affected. Of course, it depends critically on your genetic background.

For the people who are ApoE4 positive, who carry the allele for Apolipoprotein E epsilon4 (ApoE epsilon4) – there are about 75 million Americans who have a single copy of ApoE4 – they are at about 30 percent lifetime risk. Those with two copies are at over 50 percent lifetime risk. The majority of those people – there are 7 million of them in the U.S. – will develop this disease if we don’t do something to prevent it.

**JM:** Don’t get alarmed with those statistics, folks, because there’s a lot that you can do. We’re going to dive deep into the molecular biology. But before we do that, I want to really acknowledge and help Dr. Bredesen expand on how he came into this field, because, folks, he is a true anomaly.

It is the rare exceptional physician, MD – he’s an MD by training – that comes out on the other side embracing functional medicine. He happened to do it independently, outside of any functional medicine training, because there are training programs that do that. Interestingly, he started his journey into Alzheimer’s at Caltech in his freshman year. But it’s a really interesting story, so I’ll let him share it.

**DB:** Sure. We have been interested. I worked for Dr. Stanley Prusiner, who won the Nobel Prize in 1997 for discovering prions. When I set up my own laboratory in 1989, the idea was we wanted to understand the fundamental nature of neurodegeneration and what drives it. There’s so much interesting information about what drives cancer, but there had not been simple models that you could actually use in the laboratory to study what drives neurodegeneration.

We’ve spent 28 years in the lab now studying this phenomenon of neurodegeneration. We were not aware of the brilliant work of Jeffrey Bland, David Jones, Mark Hyman, David Perlmutter and all of their colleagues in functional medicine. We really came to this from a very different background.

What we discovered is that the central molecule involved with Alzheimer’s disease – of course we also studied the amyloid of Alzheimer’s – but the surprise was this thing, of course, comes from an amyloid precursor protein, or APP. We discovered a new kind of receptor back in 1993. We called these “dependence receptors.” These are receptors that actually create states of dependence on trophic factors, on hormones, on things like that. If they don’t get the appropriate
factors, then they induce programmed cell death. They induce neurite withdrawal and things like that.

The surprise was that APP actually looks like a dependence receptor. We started looking at this further. What it turned out to be is that APP actually is an integrator. In other words, it’s not just waiting for one molecule. It is summing over many different things.

Whether it is going to give you the signals that indicate that you should go forward, make synapses and keep memories, or the opposite – pull back, forgetting, activation of programmed cell death – depends on a whole set of signals. These include estradiol, progesterone, pregnenolone, free t3, NF-κB and inflammation. We realized this is what the epidemiologists have been telling us. This is, in fact, what functional medicine does.

What happens is if you look at the molecules involved, you can’t escape the conclusion that a functional medicine approach is an optimal approach. This in no way says that you shouldn’t develop drugs as well, but you want to test the drugs on a background of the appropriate program. We tell the patients, “Imagine you have 36 holes in your roof – because we initially identified 36 different mechanisms involved – if you patch one hole, that’s not going to help you that much. You want to patch all the holes.” Now, a drug typically patches one hole. You’re going to test your drug, fine, [but] patch the other 35 as well.

**JM:** Yeah. [inaudible 07:22] you should acquire here with the drugs. I’m not a fan of virtually any drug. There’s rarely – there are some, I’m sure, because the absolutes are rarely ever true. But most of the people watching us are not drug fans. It’s not an issue.

But in your research, you essentially determined that there were essentially three subtypes of Alzheimer’s. Two of them are actually not really an illness. They are strategic programming downsides of the synaptic density based on a mismatch of a number of different inputs, but essentially not illnesses.

If you implement many of the strategies that you’re recommending, you can reverse those. The point is not to get too distressed if you come down with signs and symptoms of Alzheimer’s, because there’s a good chance that it may not be Alzheimer’s. You have to look at these other subtypes. Can you elaborate on that and also provide us with the approximate percentage in each of those?

**DB:** Sure. What we found when we realized that all of these different inputs actually affect a critical balance. You can think about it exactly the way you need to think about osteoporosis. You’ve got osteoblastic activity. You’ve got osteoclastic activity. It’s an imbalance in those two over your life that leads to osteoporosis. What we’re seeing is no different. We realize this is synaptoporosis. There is synaptoblastic activity and there are dozens of signals that feed into synaptoblastic activity.

**JM:** Sorry. Let me interrupt you there for a minute, because some of our viewers are not medical professionals. Actually many and most of them aren’t. The synapse – Maybe you can expand on that so that they’ll know what we’re talking about.
DB: Right. In your brain, the critical power you have to make decisions, to speak, to learn and all of these has to do with the connections between the brain cells. You have 100 billion neurons. That’s 10 to the 11th neurons in your brain. Each one has, on average, nearly 10,000 connections. Just like the connections you have with your various listeners and with your various colleagues and so forth. These are critical for the interactions – storing memory, making decisions, all these sorts of things. You can’t do anything without these. These connections are called synapses.

When you get Alzheimer’s, you lose initially the function of the synapse, and ultimately the structure of the synapse. Ultimately, the cells themselves actually die away. You have this amazing computer inside your skull that has nearly one quadrillion connections.

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What we discovered is that there are active signals in which the pre- and post-synaptic elements, literally the two pieces come and talk to each other. In fact, this has been likened to a marriage. There is a courtship. There is a commitment. These things interact with each other. And then, of course, there is a functional and dysfunctional interaction. They talk to each other in a positive way. They talk to each other in a negative way. Unfortunately, there can be divorce. You can actually lose these synapses.

In Alzheimer’s, what we discovered is that everybody with Alzheimer’s is on the wrong side of the balance. In other words, their synaptoblastic activity is too low, and/or their synaptoclastic activity is too high. We want to go after all of those different things. Now, when we then started to measure these, we realized that you’ve got to measure things that aren’t measured in clinical practice. This has been the big problem.

People say that Alzheimer’s disease is mysterious. There’s nothing you can do about it. That’s because they have not looked at these larger datasets. Going back to what you said earlier, this is part of the new medicine. We need much larger datasets. We have a massive complexity gap right now. We’re dealing with extremely complex organisms – ourselves – and yet, we are not looking at the data that we need to be able to make the critical decisions about those organisms.

JM: I’m wondering, with the rapid development of deep learning and artificial intelligence, if you are establishing any collaboration with these groups to elaborate these massive datasets.

DB: Exactly. Yes. In fact, we’ve talked to various groups – IBM Watson, the 1492 group at Amazon, of course, Institute for Systems Biology, led by Lee Hood and Nathan Price. They are, as well, interested in larger datasets and how we can look both preemptively and, of course, for reversal. We now argue that you can, for the first time, both prevent and reverse cognitive decline. Actually, we published the first paper, as you know, that showed reversal of cognitive decline.

JM: We will definitely get into that.

DB: Yeah. The bottom line is we need to look at larger datasets. When you do that, you can see very clearly with these larger profiles that there are subtypes. So there are people who have a
predominantly inflammatory picture. We call this type 1. These people have high high-sensitivity C-reactive protein (hs-CRP), interleukin 6 (IL6) and tumor necrosis factor alpha (TNF-α) – all those sorts of things that reflect this chronic inflammatory state.

Interestingly, when you activate NF-κB as part of inflammation, what does it do? Of course, it alters gene transcription. Two of the genes it turns on are the beta-secretase and gamma-secretase that specifically cleave APP and drive it toward this synaptoclastic direction. You can see a direct link between inflammation and the production of Alzheimer’s disease in the amyloid.

Type 2 – very different. Type 2 is an atrophic response. In fact, what happens is if you want to push your APP in the direction of giving you the amyloid and giving you Alzheimer’s cell signaling, you can either induce inflammation or you can withdraw trophic support. If you withdraw nerve growth factor; brain-derived neurotrophic factor (BDNF), estradiol, testosterone or vitamin D – the list goes on – this is summing these inputs.

It’s basically functioning like your company’s CEO. It’s saying, “Do we have enough to stay in the black?” If not, what’s the first think that happens in your company? You say, “We’re not going to hire any new employees.” That’s exactly the same thing that happens in your brain. You say, “We’re not going to add to what we already have. We’re going to still be able to drive a car, to speak, etc., but we will not be able to learn new things.” That’s exactly a very common presentation, as you know, for Alzheimer’s disease. We call that type 2, atrophic or “cold” Alzheimer’s.

By the way, the Ayurvedic physicians knew about this years ago. Of course they didn’t call it Alzheimer’s. This was millennia ago. But they called this “vata.” This was the “vata” type of dementia. And then the third type is a very interesting type because it is quite different than the other two. This is a toxic type of Alzheimer’s disease. We initially discovered this because there was a set of patients who were not responding well to reducing their inflammation and improving their atrophic status. They still wouldn’t get better. We started looking further into their histories, into their laboratory data.

What we discovered is that these are people with toxic exposure, many of them having the chronic inflammatory response syndrome (CIRS) markers that Dr. Ritchie Shoemaker had described, of course. Although, interestingly, most of them do not fit the criteria for CIRS. We had to come up with something different.

They act like CIRS patients with dementia. They have high transforming growth factor beta (TGF-β). They have high complement component 4 A (C4A). They have low melanocyte-stimulating hormone (MSH). They have high matrix metallopeptidase-9 (MMP-9). They have the human leukocyte antigen-antigen D related q5 (HLA-DRDqs) that are associated with bio toxin sensitivity, often the so-called dreaded HLA-DRDqs. Yet, they usually do not have the pulmonary complaints, the rashes, the fibromyalgia, the chronic fatigue and these sorts of things. When you treat their CIRS-related –

**JM: CIRS again is what?**
DB: Good point. Chronic inflammatory response syndrome, as defined by Dr. Shoemaker.

JM: Okay.

DB: When you treat those, then they get better. Without treating them, they continue to decline. That’s type 3.

I should add just that there is a type 1.5, which is in between, because it has part of the type 1 – it’s got the inflammation – and part of the type 2 – it’s got the atrophy. Of course, these are the people who have insulin resistance, which gives them the type 2, and they have the inflammation associated with advanced glycation end products and things like that, so that they have some type 1. This is very common and, by the way, very treatable.

JM: Are these types generally recognized in conventional medicine and referenced in the literature? Those three types?

DB: They are. We’ve published two papers on these types. They are not generally accepted yet, so people are still gathering small datasets and saying, “This is a mysterious disease. We don’t know where it came from.”

JM: Okay. In your descriptive classification then, I’m wondering where the genetic one [is]. It wouldn’t be toxic, but is there another merger between type 1 and type 2?

DB: Good point. With respect to genetics and Alzheimer’s, as you know, on the one hand, about 95 percent of cases of Alzheimer’s are not so-called “familial” Alzheimer’s disease. Those are relatively uncommon. Actually, mutations in APP itself are very rare causing Alzheimer’s. They tend to be very clearly clustered in families. They come on early.

However, about two-thirds of the people who have Alzheimer’s do have one or two copies of ApoE4. In that case, the genetics of risk for Alzheimer’s is very important. Now, the ApoE4 interestingly increases your risk for type 1. It increases your risk for type 2. But it actually seems to decrease your risk for type 3, the toxin-associated one. Which is very interesting because, as you probably saw just a few days ago in the New York Times, there was a piece on ApoE4 as being protective with respect to parasite-associated dementia. This actually was from a paper that appeared back in December.

In fact, ApoE4 is protective for certain things. It is a more pro-inflammatory state, so very good for dealing with things like microbes. Not so good later in life, thus a case of what’s called antagonistic pleiotropy. It’s good for you. It helps give you advantages when you are young, but it is a liability with respect to chronic illness and lifespan when you are older.

JM: Yeah. I first encountered your work through one of the presentations you gave at STEM-Talk. I was really intrigued when you talked about the ApoE4 being actually protective, not for Alzheimer’s, but it’s a useful allele to have. It’s a very powerful strategy for your body to stay alive. What does it do? We’re really going into what you said because I never was aware of this before. But it helps you survive during times of low food, which is not the case for most of us.
It occurred to me – and I want you to obviously expand on this – that if you got this – you can determine it, obviously we can do genetic testing inexpensively – then, to me, this would be a strong clinical indication that you absolutely need to do intermittent fasting and regular fasting on a regular basis, unless you want to expose yourself or predispose yourself to this illness.

**DB:** This is absolutely the case. I think it’s a very interesting point. ApoE is such a remarkably interesting gene. The ApoE4 was the primordial gene that appeared between 5 and 7 million years ago. If you look at chimps for example, they do not have the same ApoE as the hominids. This seems to have appeared with the hominid evolution. For 96 percent of all of evolution of hominids, we’ve all been ApoE4 double positive, so homozygotes. This is the genetic status that we associate with Alzheimer’s disease.

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**JM:** Oh gosh.

**DB:** It’s only been the last 4 percent of our evolution that ApoE3 appeared—220,000 years ago. ApoE2 appeared 80,000 years ago. Very interestingly, ApoE4 prepares you to change niches. When we moved from in-the-trees arboreal ancestors to walking on the savannah, stepping on dung, puncturing our feet, eating raw meat filled with microbes, we needed a pro-inflammatory gene.

In fact, if you look at the genes that are different between simians and hominids, in fact, a surprising number of these are pro-inflammatory. As you indicated, ApoE4 also allows you to eat fat, absorb it better and go longer without eating. If you take people who are ApoE4-positive and -negative and starve them, the ones who are negative will tend to die earlier. Therefore, it’s not that it’s better or worse. It’s different. It gives you some advantages. It gives you some disadvantages.

Therefore, you can learn to live your life slightly differently that is of advantage to you. My argument is nobody – If you really do the right things, Alzheimer’s disease should be a very, very rare illness.

**JM:** I couldn’t agree more. Now, you put together something called the MEND Protocol, which is Metabolic Enhancement of Neurodegeneration. You may not be aware, but I wrote a book this year called *Fat for Fuel: A Revolutionary Diet to Combat Cancer, Boost Brain Power, and Increase Your Energy.* It really focuses on something called MMT or what I call – I made it up – Mitochondrial Metabolic Therapy, but I think they’re pretty similar processes.

You’ve identified dozens – maybe four dozen or more – variables that can really have a significant influence on this disease. I’m wondering if you think that the common pathway, the mechanism, is essentially through mitochondrial dysfunction, establishing some disruption of the mitochondria.

**DB:** No question. Mitochondria play an important role. But again, as you indicated – By the way, my wife just finished reading your book.
JM: I’m honored.

DB: I’m reading it. She’s a family practice physician. Actually, she’s taught me a lot about functional medicine.

JM: Great.

DB: She told me 25 years ago, when we were in the lab, “You know, whatever you guys find is going to have something to do with diet, exercise, sleep and stress.” I told her, “Absolutely not. I’m a molecular biologist. We’re going to have one domain of one little molecule that’s going to do everything and so forth.”

JM: That’s why you’re such an anomaly.

DB: I should have listened to her. I should have listened to her.

JM: But you followed the facts, [unlike] so many people. I think it’s because of pride. They’re just so unwilling to abandon the truth once they find it. That wasn’t your case.

DB: When you see people starting to get better from Alzheimer’s disease, you cannot refute it. You see people improving their scores. You see people going back to work. You see them becoming part of their families again. You just can’t refute what you see. You can’t refute this sort of approach.

I should say, it’s a toe in the water. These are early days. This is the beginning. But it gives us a place for the first time to start and to say, “Okay. Now, how can we optimize this? How can we get better and better and better?” What’s really interesting – We agree that certainly mitochondria are huge. Again, if you look at –

JM: There’s a quadrillion of them, just as many senescent cells that you have.

DB: That’s a really good point. If you look at what changes the most between birth and death, what is senescence all about? We lose some muscle mass. We lose the ability to make hormones, all these things. The argument has always been the thing that changes the most – it’s five to six orders of magnitude – is mutations in mitochondrial DNA. That’s the thing that collects the most as we age.

JM: That’s where the energy is produced. That’s where the free radicals are generated, the majority of them. It’s exactly what you’d predict.

DB: That’s a huge issue. And yet, at the same time, as you well know, functional medicine shows you’ve got to look at this as a coordinate unit. The mitochondria are working with us. They invaded us many years ago and they’re our friends. Of course, we and they can be enemies at times. You’ve got to support the whole thing. You’ve got to look at the inflammatory state. You’ve got to look at the glucose state. You’ve got to look at insulin resistance.
One of the biggest surprises we found is that if you look at why APP is actually making these amyloids, it’s actually changing the synaptoclastic side. The very amyloid that we have vilified and tried to get rid of turns out to be – surprise – a protective response to three fundamentally different classes of insults. These go along with the subtypes of Alzheimer’s.

If you’ve got inflammation going on, you are making the amyloid because, as Dr. Robert Moir and Dr. Rudy Tanzi from Harvard showed, it is an antimicrobial, a very effective endogenous antimicrobial. If you are decreasing your trophic factor support, as my laboratory showed years ago, APP is a dependence receptor. You are downsizing a network. As you mentioned earlier, in that case, it’s not really a disease. By the way, I saw that you had Professor Mike Merzenich, a colleague and friend.

JM: Sure. It was a number of years ago, but he was a good guy.

DB: Mike says, “Hey. This is not a disease. This is a falling apart of the system.” You’re making amyloid because you’re fighting microbes, because you’re under assault and you’re inflamed, because you are decreased in your trophic support (insulin resistance, etc.), or because, guess what else amyloid does beautifully? It binds toxins, like metals, mercury and copper. It’s very clear you’re making this stuff to protect yourself. It’s all well and good if you want to remove it, but make sure to remove the inducer of it before you remove it. Otherwise, you’re putting yourself at risk.

JM: Alright. Before we jump into some of the clinical recommendations that I’d like to really delve into, because there are some that I haven’t seen highlighted in your research. I want to jump back into the genetics and have your response to the conventional media’s approach.

I mean 60 Minutes just reran a story that ran in November about this family. I forget the name of the syndrome, but they were really – it’s some family there in Colombia where the drug cartel was – they were hoping to learn or essentially identify drugs to treat it. When PBS does their documentary on the tsunami of Alzheimer’s, there’s not a darn thing we can do about it. That’s the conventional wisdom of the media, and I would assume most researchers in this field. I’m wondering if you can comment on that.

DB: Absolutely. The current status, as you know, is that this is a mysterious illness. It can be genetic, which is rare. This family has presenilin 1 (PSEN1) mutations. The hope is that we would use a specific drug and test these drugs to see if we can prevent it. Here’s the problem. APP, as we talked about earlier, is like a CEO essentially. It’s looking at all the inputs from both sides, the pro and the con. It’s deciding, “Are we going to be able to make more memories? Are we going to have a positive synaptic plasticity? Are we going to be synaptoblastic or are we synaptoclastic?”

Now, in the few families that have this, they are pushed towards the synaptoclastic side, from the beginning. That is not representative of what over 95 percent of us have. We are pushed there appropriately because we ate the wrong foods, we stayed up too late, and we abused ourselves in so many ways with stress. We ate the wrong things. We were exposed to all these toxins. We
lived a Western lifestyle. We ate the standard American diet. Our hormones decreased. Those are the things that are driving our APP to produce the synaptoclastic side.

In those presemilin1 cases and in the APP mutations, it is not the same mechanism. Unfortunately, the mouse models that we all work with are like familial Alzheimer’s, not like the sporadic Alzheimer’s, which is the vast majority. Now, this is not to say that the drug cannot work. Let’s hope for the best. But again, I would argue that you want to address the various things that are contributing to an appropriate response of your APP, which we ultimately call Alzheimer’s disease.

**JM:** Okay. Great. Thank you for that expansion, because I wasn’t sure of the total perspective about the 95 percent. It was really helpful.

Now, I’d like to delve into some treatment strategies. Hopefully, you’re willing to share, unless it’s proprietary – we can coast in on this – is that your MEND variables that you look at and address in the actual lab test that you use to monitor like hs-CRP, vitamin D, pregnenolone and a whole variety of other factors. But I’m not sure that you’re checking for these.

Even if you are, I’d like to have your comments on them, because as I was doing the deep dive in the molecular biological research in writing my book, it became very clear to me that the name of the game is to preserve mitochondrial function. One of the best ways to do that is to radically reduce or optimize free radical stress in the mitochondria.

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One of the ways that you can do that – and certainly not the only one – is to give it its preferred fuel source, which I believe is fats and, more specifically, ketones, and ideally optimizing the cyclical fashion. Because if you do anything persistently, it’s likely not to be good. Pulse cyclical ketosis. I’m wondering if you’ve looked at that or [you’re] using that strategically in your interventions or what your thoughts are on it.

**DB:** Absolutely. Let me start by saying the original protocol we developed, [which] I dubbed MEND, metabolic enhancement for neurodegeneration. That is now several years out of date.

**JM:** Okay.

**DB:** We continued to evolve it. Yeah. It’s okay. This is all explained in the book, which is coming out on August 22nd.

**JM:** Cool.

**DB:** Yeah.

**JM:** When is your book coming out?

**DB:** The book is coming out from Random House. It’s coming out August 22nd.
JM: I did not know that, but it’s fortuitous because we’ll hopefully be able to accelerate this and have this launched for your book, to help your sales for that.

DB: That would be great. Thanks so much, Dr. Mercola. I appreciate that. What happens is it’s what we now call ReCODE. ReCODE is “Reversal of Cognitive Decline.”

JM: Okay, so you’ve changed the name. Okay.

DB: Yeah. We’ve continued to evolve it. This is an evolving strategy as we learn more. Absolutely, as you’ll see, if you ever look at a ReCODE report – we have a computer-based algorithm that we’ve developed – the most important part is just what we talked about earlier and what you alluded to just a minute ago, which is to get an evaluation.

The critical piece here is not to say, “Oh, you have Alzheimer’s. We don’t know why.” The critical piece is to say, “How can we leave no stone unturned? Because if we don’t do something about this, this is a terminal illness. Let’s look at all of the contributors to your cognitive decline. We know ahead of time that because of the cognitive decline, you have this change. If it’s what we call Alzheimer’s, you, by definition, have a change in your APP signaling with the occurrence of this amyloid. Let’s look at all the things that contribute to that.”

You’re right, there’s a lot written about free radical contribution to this. We recommend that everybody induce mild ketosis. We recommend that they get ketone meters and stay between 0.5 and 4 millimolar beta hydroxybutyrate. There’s been some interesting back and forth about whether it’s better to do with the breathalyzer or with urine. So far, as you know, measuring the beta hydroxybutyrate seems to be the most standard way to go.

JM: Yeah. But pragmatically, the breath analyzer is the way to go. Who wants to stick themselves or pay the expense? Pay 4 dollars a stick, you know?

DB: I completely agree with you there. Hopefully, one day we’ll have an optimal way to do this that satisfies everybody. But for now, you’re right. There’s a pragmatic issue here. What we do is we look through ReCODE. We look at all of the contributors.

Interestingly, if you go to an advanced cancer center today and you have a tumor, what do they do? They biopsy the tumor, and they sequence the entire genome of the tumor. They sequence your entire genome and they compare them. They say, “Why did this person get this tumor? What are the things that drove it?” What we do is exactly the same thing. The difference is we don’t have a tumor to biopsy, of course.

What we do then is we look at 150 different variables right now, which include biochemistry, genetics and volumetric imaging. This gives us a very good look at what is actually driving this. We take these 150 variables. We feed them through the algorithm. It will then generate for you what percentage of each subtype do you have. Because, in fact, most people aren’t pure type 1 or pure type 1.5 or pure type 2 etc. Most people have a dominant one, but then contributions from some of the others.
Then, yes, of course, after you can tell, “Okay. Here’s what this person should do.” It’s different for each person. It’s personalized. If you have insulin resistance, which many people do, as you know very well, you want to address your insulin resistance. You want to create insulin sensitivity. You want to decrease your inflammation. You want to remove the source of the pro-inflammatory effect. You want to remove toxins.

As you know, Dr. Joseph Pizzorno has done a great job of looking at all these different toxins that we are exposed to. It is, indeed, a toxic world in which we live. We need to enhance the ability to evaluate these, identify them and remove them ultimately. This is a fundamentally different way for looking at what’s causing this.

As you indicated, there’s a tremendous amount you can do. We recommend that everybody over the age of 45 get what we call a “cognoscopy.” We all know you’re supposed to get a colonoscopy when you turn 50. If you’re over 45, think about getting a cognoscopy. It’s very simple. You’re going to look at these different things in your blood. You’re going to look at your genetics. You’re going to look at your function. You can do quick online screening from groups like Dr. Merzenich’s Posit Science in BrainHQ. There are other ways to do it – Cogstate, for example. There are many different things for this, to look at your status. Then get on the appropriate program for prevention.

If you’ve already started to be symptomatic, get on an appropriate program for reversal. The earlier, the better. As you alluded to, yes, it includes diet. We absolutely suggest mild ketosis, mostly plant-based. The diet we use is called KetoFlex12/3. I want to thank Julie Gregory and my wife, Dr. Aida Lasheen Bredesen, for the tremendous amount of work that they’ve done on, particularly for the KetoFlex 12/3 diet, optimizing it and, in part, it is based on neuroprinciples. This is critical.

Exercise, increasing your BDNF. There are, of course, new ways to do this, such as the so-called whole coffee fruit extract that actually David Perlmutter first introduced me to, and other ways. Stress is critical. Sleep is one of the most ignored things that are absolutely critical for your cognitive function. And then, there’s a whole host. You have a very large armamentarium. You need the appropriate magnesium levels. You need the appropriate vitamin D levels. These are optimal.

I always tell the patients, “We’re going to treat you now like a competitive athlete. What you’re doing is not working. You are slipping into Alzheimer’s.” We want to optimize these things. When you do that, the effects are absolutely striking. I would see people go back to work. One person said, “I’ve allowed myself to talk to my grandchildren, once again, about the future, because I had to stop doing that.” One person went from 3rd percentile to the 84th percentile on his cognitive testing. Another person had increased hippocampal volume dramatically. These are unprecedented effects, because we are addressing the specific items that are actually causing the cognitive decline.

**JM:** Terrific. Just a slight disagreement with some of your analogies with respect to what conventional medicine does, not your viewpoint of them, but they do this genetic sequencing of the tumors.
One of my heroes is one of Dr. Thomas Seyfried, who wrote the book *Cancer as a Metabolic Disease: On the Origin, Management, and Prevention of Cancer*. He would strongly disagree with that because, yes, there’s genetic damage, there’s no question, but it’s a secondary downstream side effect from the metabolic arrangement of the damage to the mitochondria. Then the colonoscopy – there are so many problems with that, especially the disinfectant they’re using, the glutaraldehyde. [inaudible 37:57] They’re some minor issues.

**DB:** We don’t use any glutaraldehyde in our cognoscopy.

**JM:** Good, good. That’s good to know. The other thing on the ketosis, I don’t know if you’re recommending or incorporating it to your program, but I learned from really personal experience and lots of experience from others that it really can’t be continuous. You will get good improvement initially, but then you’ll start to decline. You’ve got to bounce out of it like twice a week with relatively high amounts of carbs. I think this may go into one of the other components.

I’m not sure if you’re addressing it with your specific dietary recommendations, but there’s no question in my mind that the microbiome is intimately related here. I think that’s part of the reason why the cyclical ketosis works. It’s that it feeds them so well and it produces these short-chain fatty acids. One of the things I’m looking – well, there’s a lot of things we’re looking at, like molecular hydrogen production from the microbiome and certain fibers that will do it.

My training as a resident – I don’t know if you trained in the inner city like I did – but I had a lot of patients with hepatic encephalopathy. Probably this was in the ‘80s, I’m sure they were using lactulose, you know, this synthetic non-digestible disaccharide that works like unbelievable. How could this thing work? Now, I think we know the mechanism. It produces a heck of a lot of molecular hydrogen, which improves brain function.

That was a long tangent, but I’m wondering if you looked at any specific fibers. That’s one of my passions. I want to tweak this and understand these other fibers, because lactulose is a drug. It’s prescription. We’re the only country in the world where it’s prescription. Almost everywhere else, it’s not. But there’s got to be other fibers that can deduce similar benefits.

**DB:** That’s a really good point. Just to start with the microbiome that you mentioned, what we found is that the microbiome is absolutely critical, as you know, and leaky gut. One of the things that is part of the cognoscopy is to know whether you have a leaky gut.

[-----40:00-----]

One of the interesting things is we’re finding that not only is the gut microbiome critical, but the rhinosinal microbiome. What’s going on in your nose and sinuses is absolutely critical.

By the way, when you look at the brain of patients with Alzheimer’s, you find an increase in a number of pathogens. What are they? They are oral bacteria, like P. gingivalis, Herpes simplex virus-1 (HSV-1) from your lip, molds that are coming here from your sinuses. This region has access to your brain. And of course, there are other things systemically, like Lyme disease. Then,
of course, changes in the gut have been associated both with Alzheimer’s and Parkinson’s. The microbiomes are absolutely huge. We include healing of the gut. We include probiotics and prebiotics.

As far as specific fibers, we suggest, as you know, that it’s critical that you have this. As Dr. Lustig has pointed out, it’s critical that you include both the soluble and the insoluble fibers. But as far as specific ones other than the fact that it’s critical to get these in your diet if you can, we have not yet recommended any specific fiber, one or the other. In fact, as far as the cyclical ketosis, we’re learning this from you. Thank you for that. There’s no question, ketosis helps.

**JM:** Thank you. I’m glad you are integrating that, because I’m fairly confident with the very small degree of – I’m just fairly confident that it’s going to be correct.

Now, I’m curious personally. A physician’s, Mary Newport, husband passed from Alzheimer’s. I’m sure you’re aware. She used a lot of coconut oil in the beginning, and then eventually switched over to MCT oil, and then exogenous ketones produced by Dr. Richard Veech. Unfortunately, it was a little bit too late at the last minute. But I’m wondering if in your program if there’s a place for exogenous ketones, especially the ketone esters, which are more expensive, in severe cases, if you’re integrating that to the program.

**DB:** It’s a great question. It’s something we’ve been looking into. In general, we have used a combination of the specific diet, specific fasting periods, much like the fasting periods you’ve described. That’s the origin of the 12/3 part of KetoFlex 12/3. It’s a minimum of 12 hours.

**JM:** Excuse me for interrupting, but do you increase that or make it mandatory if they’re ApoE4-positive?

**DB:** Yes. If you’re ApoE4-positive, we recommend 14 to 16 hours instead of the minimum of 12.

**JM:** Interesting. What’s your best recommendation to the first screening test? Is it a screening test for the ApoE4?

**DB:** There are a number of things you can do. 23andMe is fine. 23andMe will report ApoE allele status about 85 percent of the time. They’re not always able to get your ApoE status from a sample. But it’s relatively inexpensive to do it that way. There are now many other groups that do it. That’s certainly very reasonable to do.

We do look at specific fasting periods. And, yes, there is absolutely a difference about whether you have ApoE4. Again, you are a different organism. One of the things that we discovered and published was that ApoE does something that hadn’t been recognized before. ApoE, as you know, is a fat-carrying molecule. It’s a little bit like a fat bucket. It’s a little bit like your butcher. It carries around the fat. What the heck does that have to do with Alzheimer’s disease? We started looking at this.
Now, eight years ago, looking at why do you start with ApoE4 and end up with Alzheimer’s. What’s in the black box in the middle? It turned out, surprisingly, that ApoE actually enters the nucleus. It binds to the promoters of 1,700 different genes. It literally reprograms your cell toward a more inflammatory state. In fact, if you look at the groups of genes, you couldn’t tell a better story about Alzheimer’s. It binds to things related to neurotrophic support, synaptic growth, inflammation, etc., which are all these sorts of things that we talked about earlier. ApoE has a big impact.

**JM:** Great. Now, I’ve got two last interventions that I suspect you aren’t doing, but if you aren’t, I would encourage you to look into them. One is based on the work of Michael Hamblin as a PhD out at Harvard and really an expert in photobiomodulation where he uses near-infrared light, and actually red, so about 660 nanometers and 830 or so, somewhere in that range.

Lew Lim is an MD out of Canada, I think Toronto. He’s developed a device called the Vielight, which essentially are light emitting diodes (LEDs) at these frequencies. Mostly they’re infrared, near-infrared. Twenty minutes a day and it just had unbelievable results. It’s just near-infrared light. Its toxicities and side effects are pretty minimal. I’m wondering if you’ve looked at that or planning to integrate that into the program.

**DB:** Absolutely. I’m aware of the work, very interesting work. We’re looking into it, as I’m sure many others are. I think we’ll know. We’ll have some data coming up.

**JM:** Yes. You’ve got the parameters to guide it and measure it.

**DB:** Absolutely. One of the big issues has been how do you look at a coordinate system that uses, of course, the classic way. By the way, this all started because we tried to do the first comprehensive trial for pre-Alzheimer’s, so-called “mild cognitive impairment” (MCI), back in 2011, which had all these different pieces to it. The institutional review boards, both public and private, turned us down because they said you have to test one variable at a time. Unfortunately, that’s not the way these chronic complex illnesses work.

But a way forward is you start with a specific part of your plan. It might take 10 things, 15, 20, get to a plateau, and then you can add and subtract. Once you have a plateau, you can say, “Okay. If I add infrared light, does that help? If I subtract something, does that hurt?” So then you actually have a way to go. When you start with nothing, the so-called floor effect, you don’t know if you’re having an effect that you can’t measure yet. You need to get to a dynamic range so that you can actually see changes with single variables.

**JM:** Good. I’m glad you’re interested in that. The last part I wanted to bring up was one that I’m sure you’re aware of. But you may not be aware of the molecular mechanism, because it was just published a few years ago. That is electromagnetic field (EMF). I’ve known about it for a long time, but never realized the relative importance of it as being perhaps maybe the most pernicious toxin of all, because of the exponential exposure that we continue to have, especially with 5G implementation in the next two years. Are you familiar with Dr. Martin Pall’s work? P-A-L-L?
DB: I’m familiar with the EMF issues. When we look at people, we look at biotoxins, we look at chemotoxins, and then, of course, physical toxins.

JM: Okay.

DB: EMF’s critical.

JM: Yes. But his work has to do with the voltage-gated calcium channels. Are you familiar with that?

DB: Yes.

JM: Okay. Good. You know that it ultimately results in excessive free radicals through the introduction of calcium, nitric oxide, super oxide and foreign peroxynitrite and then hydroxyl free radicals. It would seem that if you can mitigate against that and I think the first step like in anything, any strategy or disease treatment program and prevention, is to get a meter and go around your house.

I’ve recommended this to a few physicians. They’ve gotten the meters. Every single one of them, including myself, has found no less than three hidden sources of EMF that were massive in their home and they were completely unaware of. You can intellectually understand it, but when you have a meter and you go around, that makes a big difference. Minimizing that and also looking at other – I mean there’s going to be some EMF exposure you’re just not able to mitigate, because there’s a certain threshold level.

But if, in fact, the generation that this EMF impacts you and impacts the cells and the cell damage – The other reason why it’s so important to Alzheimer’s is these voltage-gated calcium channels, the highest density is in the brain tissue. Of all the tissues in the body, it’s in the brain. It’s exactly a tissue you’d expect to deteriorate rapidly from exposure.

Dr. Pall figured this out by reviewing these studies. Actually, they were mostly in-vitro studies and some animal studies, but they used calcium channel blockers. When there are calcium channel blockers, they expose these cells to EMFs. They didn’t have the side effects. Obviously I’m not a big drug fan, but magnesium could be a strategy, and then also perhaps using molecular hydrogen to mitigate it selectively against those hydroxyl free radicals.

DB: It’s interesting. There’s already been a study published by Dr. Guosong Liu from MIT. He runs a laboratory back in China. I discussed this work with him. He’s using magnesium threonate and has shown improved cognition.

JM: With Alzheimer’s?

DB: With cognitive decline. These people don’t necessarily have a diagnosis of Alzheimer’s, but they were people with cognitive decline.
JM: There are other reasons that may work, but it's interesting that it may be blocking those calcium channels.

DB: It's possible. Of course, sodium channels are also critical. Levetiracetam is a drug that is now being evaluated because of sodium channel activity, and because of the fact that many people will have sub-threshold seizures by electroencephalogram (EEG) activity. You're having essentially electrical seizures without actual tonic-clonic seizures. In fact, as you indicated, there is abnormal electrical activity and associated channel alterations in the brain of people with cognitive decline.

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JM: Terrific. Do you have a resource that we could link to that has a list of all these variables? Because I've listened to a number of your presentations and I've read a number of your papers, but I could never find a complete list. Or is it in your book? The name of your book again?

DB: The book goes through the complete background of it. The book has actually been named by Random House, *The End of Alzheimer's: The First Program to Prevent and Reverse Cognitive Decline*. I have to say, I sent 10 different titles. They didn't like any of my titles. They did their “market research,” and came up with *The End of Alzheimer's*. My concern, of course, is the end of poverty, the end of hunger, the end of war.

JM: Sure.

DB: But the hope is that when we all work together, we can make a major impact and reduce this. As I said, it should be a rare illness. That is the truth. It should be a rare illness if we do the right things, if everybody gets the appropriate cognoscopy. This will come out August 22nd from Random House Avery.

JM: Okay. Good.

DB: This goes through all the different evaluations.

JM: Yeah. Perfect. That’s exactly the solution, because I really did need it to be put in one place. In fact when I was reviewing your materials I said, “Why don’t you write a book?”

DB: Yeah.

JM: Is this your first book?

DB: This is the first one about this. We wrote something about non-apoptotic cell deaths that you may not have read.

JM: Okay.

DB: Other than my mother, there weren’t that many people who bought that one.
JM: Sure. Well, with respect to the title that the publishers assigned to your book, let me share something about my first book, which was *The No Grain Diet: Conquer Carbohydrate Addiction and Stay Slim for Life*. I abhorred the title. I absolutely abhorred it and regretted that I relented to letting them use that title up until a few years ago. Then I’ve come full circle and I thought, “It probably was a really good strategy.”

That’s actually another point I want to discuss, because I don’t know if you’ve integrated this brilliant clinician’s work into your program. If you haven’t, I would highly encourage you to do it. That’s Dr. Steven Gundry. He wrote the book *The Plant Paradox: The Hidden Danger in “Healthy” Foods That Cause Disease and Weight Gain*.

DB: I’m also reading that right now. It’s actually sitting about 5 feet from me.

JM: Yeah.

DB: I like Steven’s work.

JM: Yeah. Brilliant. Really brilliant. Lectins, they’re going to cause inflammation, which is the first subtype, I guess, of your classification. I hadn’t read it. I was aware of lectins but never knew the importance when I wrote my book, otherwise it would have been in there. I suspect it’s not in your book because you just started reading it now too.

DB: Well, you know, it’s interesting. I had actually read an advanced copy of Steven’s book, but I didn’t put it in because I didn’t know when his was going to come out and I didn’t want to say something. This was his discussion. I think he does a great job with it. With respect to the title issue, no question. Random House knows titles of books far, far better than I do, so I yield to their greater knowledge and experience in this area.

JM: I think it may be true. In 2004, I wrote my book *The No Grain Diet*. It was a bit controversial. But now, it’s becoming really clear, so that’s why I’m happy with it. I really believe that in a decade or two, as the epidemic continues to increase, a significant number of people will tend to believe and incorporate the recommendations that you and I are putting out there. It can. These are the answers. This is the answer. It’s not just the answer for Alzheimer’s, because I’m confident that the same diagnostic strategy and intervention that you use for Alzheimer’s is good for just about any chronic degenerative disease, including cancer and heart disease.

DB: Again, looking at what’s actually contributing, this is the difference between 20th Century medicine that asks “What? What is the diagnosis?” and 21st Century medicine that asks, “Why? What are all the contributors?” Whether it’s cognitive decline, arthritis or type 2 diabetes, we want to look under the hood at all the things and you want to alter those. Just as you’re saying, you alter them with things like your diet.

JM: Well, this is great. You’ve done a wonderful job on that. I wish I would’ve had the book before I interviewed you. But, I mean, your work is out there. It’s definitely possible to get the summary of it, but it would be nice to have the details that you’re going to discuss in the book.
DB: Yeah. Thank you.

JM: Anything else you’d like to add, elaborate on or emphasize?

DB: Just that I think we are all in the middle of a revolution. I think that you and your listeners know this very well. This is a major change in medicine. Certainly very different than what I was taught back in the 1970s in medical school. We are now looking at how the human organism actually works. We are now able, for the first time, to do essentially what Jonathan Wright calls human biochemistry.

Drugs may or may not turn out to have their place. But the bottom line is we need to understand what’s causing the problem, whatever the problem that you’re looking at is. We are now dying, as indicated earlier, of complex illnesses, like cardiovascular disease, cancer and Alzheimer’s disease. This is a real revolution in the way that we think. My fervent hope is that we will see more of this in medical schools and in our universities. Starting to look at what is actually driving these illnesses, instead of the old-fashioned approach of “Let’s write them an antibiotics prescription.”

JM: Yeah. I’m not sure of the exact reasons that catapulted you out of the conventional thinking, but certainly one of the variables or the factors that contributes to the reluctance of so many conventional physicians to adopt this is the pressure they’re getting and the manipulation from the drug industry. They’re a very powerful influence. It’s difficult to get over that. But eventually, it’s going to fail, because I don’t know. Maybe some drugs are useful to help this, but they’re certainly not treating the cause.

We need as many resources as we can. But ultimately, when you address the foundational causes, that’s the best solution. It’s the most cost-effective. As our culture continues to ignore this, we’re going to suffer with this. Unfortunately, it’s going to be this massive suffering that will cause people to seriously reconsider their strategy and hopefully adopt some of the things that you’re recommending.

DB: Yes. You’d want to go upstream, physiological. Absolutely. I would suggest that instead of calling this sort of approach “alternative medicine,” it should be called “effective medicine.” That is the thing that actually makes the difference.

JM: Yeah. That’s a good way to close on. Thank you for everything you’re doing, have done and will continue to do. I’m fairly confident that your book’s going to be a big part of the reason why we will really put a dent on the explosive and exponential increase that we are experiencing and the experts are projecting. Because if we lose half the people on the beginning side through autism and half on the top side through Alzheimer’s, I mean we can’t exist as a culture. There’s just no way. We’ll collapse. There’s no other inevitability that you can project other than this utter and complete collapse. We’ve got to recover.

DB: Absolutely. Imagine reducing the global burden of dementia dramatically. Imagine what that would do for the planet.
JM: Yes. It’s just sad to see that so many of us have parents who have this. It’s just sad. It doesn’t have to happen. You can reverse it. You’ve shown that you can reverse it in the studies that you’ve published. Thanks for your work.

DB: Alright. Thanks, Dr. Mercola.

[END]