The Latest Updates on the Prevention and Treatment of Alzheimer's Disease
A Special Interview With Dr. Dale Bredesen
By Dr. Joseph Mercola

Dr. Joseph Mercola:

Welcome, everyone. Dr. Mercola helping you take control of your health and today we are joined by someone we haven't spoken with for a while, but he's clearly top in his field with respect to him being a neurologist who has put his focus and concentration on helping people with Alzheimer's disease, not only helping them but helping prevent it, which is, in my book and I think in most of our books is really the key because it's so much easier to prevent something than it is to treat it.

And Dr. Bredesen has got a lot of updates for us because it's been a few years, I don't remember when, but it's at least four or five years since we [inaudible 00:00:37], certainly pre pandemic for sure.

Dr. Dale Bredesen:

Yep.

Dr. Joseph Mercola:

That's an interesting line in the sand is before or after the craziness.

Dr. Dale Bredesen:

Exactly.

Dr. Joseph Mercola:

Yeah. I think that's the last time I saw you too. It was at a keto event I think, or a low carb.

Dr. Dale Bredesen:

Yeah, down in San Diego. Yeah.

Dr. Joseph Mercola:

Yeah, that's right. And that was about four or five years ago, but we certainly talked before then too. All right. Well, why don't you give us an update of where you're at and what's new, the new and the latest and the greatest?

Dr. Dale Bredesen:

Absolutely. Thanks, Dr. Mercola. Great. So much great stuff going on. This is a great time for an update. So number one, we've got a new trial that is starting, it's starting at six sites; Hollywood, Florida; Nashville, Tennessee; Cleveland, Ohio; Sacramento, California; Oakland; and San Francisco. Six absolutely fantastic integrated physicians, Dr. Craig Tanio, Dr. Nate Bergman, Dr. David Hussey, and Dr. Kat Toups, Dr. Ann Hathaway, and Dr. Kristine Burke. So really thrilled and honored to be working with them to do this next trial.

We've had a publication since you and I talked, Joe, last time. We've had a publication of a very successful proof of concept trial. So now this trial will be a randomized control trial at those six sites. And we will include biological aging and we will include brain aging and epigenetics. So we will include the new blood tests, so new exciting blood tests, phospho-tau 181, as you know, phospho-tau 217, the A-beta 42 to 40 ratio. These were all just not available just a few years ago. GFAP and neurofilament light.

And a couple of these are not commercially available yet, so we're doing these, of course as research, but they will all become commercially available. And currently phospho-tau 181 is commercially available and so is the A-beta 42/40 ratio. So now for the first time, you can get an idea without necessarily having a PET scan to look to see, "where do I stand?" And more importantly, you can follow it as you improve. As you mentioned, prevention is key, but also reversing cognitive decline, which we were the first to do back published in 2014. We've seen it again and again and again. When you're doing the right things, when you're attacking the important drivers of the process, you see that. And the next thing is now-

Dr. Joseph Mercola:

Well before we go to the next thing, why don't we just-

Dr. Dale Bredesen:

Sure, sure.

Dr. Joseph Mercola:

... stop on these because I am not familiar with those tests, but from their names, I suspect that they're related to the unfolded proteins that are observed to be increased when someone suffers from Alzheimer's, that would be the tau proteins and beta-amyloid I would assume.

Dr. Dale Bredesen:

So they are very much complementary. So they give you different information, which is very interesting. So for example, GFAP is not specific at all. It is just looking at brain changes that are associated with astrocytosis. So your astrocytes are responding in your brain to a problem, but it is the most sensitive. So you see this go up about 10 years before symptoms. So, we should all ultimately know our GFAP and know, are we doing well now-

Dr. Joseph Mercola:

What is that short for? GFAP?

Dr. Dale Bredesen:

It's glial fibrillary acidic protein.

Dr. Joseph Mercola:

Okay.

Dr. Dale Bredesen:

So when your astrocytes that are supporting your neurons in your brain get notified, "Hey, something's going wrong." It can be a car accident or a bike accident, it can be getting hit in the head by your surfboard, or it can be early Alzheimer's disease. The good news is if it's normal, you're in pretty good shape. And so you want to know that going forward.

And then on the other side of things, the phospho-tau 181 and soon phospho-tau 217, these are quite specific for Alzheimer's changes, but they're not quite as early. So they're very helpful to know. And it's

really telling, you and I talked before about this idea that when things are not good, you have a synaptoclastic response, you're pulling back on your synapses and you see the signals of that. And that's what the phospho-tau is showing you. When things are good, you're now having a synaptoblastic response, you're making and storing new memories and your phospho-tau is going to go way low because phosphorylating the tau is what pops it off of the microtubules and allows your neuronal processes to die back. So these are going to be very, very nice tests to have. And we've been checking this recently on everyone looking to see what their phospho-tau 181 is and as I say, soon the other ones will be available.

Dr. Joseph Mercola:

So just a few questions on these proteins to update and perhaps revise, or inform people who aren't aware of it. But typically the thought in conventional medicine was that these proteins that are seen at increased levels in Alzheimer's are the cause, and not necessarily an artifact or an innocent bystander, somewhat like the firemen at a fire. Some people could believe because you only see firemen when there's a fire, so maybe they're causing the fire. So what is your view on tau and beta-amyloid as causal factors versus just correlated with the disease?

Dr. Dale Bredesen:

Yeah, great point. And I completely agree. This is a little bit like saying, "There's some smoke there. If we just blow away the smoke, then the house is not going to burn down." It just makes no sense. So the key thing to know though is that it's not just that they are responses, they are also mediators. So the upstream response is what you get, and you've talked a lot about mitochondrial function, which is absolutely critical in this disease, but we know of many now upstream contributors, and that's another update, people have not known what's causing this disease and it's often said we don't know the cause and there's nothing that prevents, reverses, or delays. Nothing could be further from the truth. We know that there are many contributors and of course, anything that damages mitochondria, part of that, different infections.

What we now see from the research is that Alzheimer's disease fundamentally is a network insufficiency. You have this beautiful network of about 500 trillion synapses and as you get exposed to inflammation, infections in your mouth, insulin resistance, leaky gut, not enough blood flow, reduced oxygenation, reduced mitochondrial function, any of these things, what happens is that network is no longer sufficiently supported. And no surprise, it pulls back and that's why you see the tau. But what happens when you see these and why people have gone after these, they are part of the mediators of making this effect enhance. So they amplify the problem.

And Dr. Lee Hood and Dr. Nathan Price have just published a wonderful book called “The Age of Scientific Wellness.” And as they point out, amyloid is an excellent biomarker, it's a terrible therapeutic target, and that's exactly what's coming out, as you know the data, and you've spoken about this, things like Lecanemab. Unfortunately, Lecanemab was just recommended by the panel for FDA approval, but yeah, I know. It's-

Dr. Joseph Mercola:

Is that recent? Is that recent?

Dr. Dale Bredesen:

Yeah, just last week. Yeah, last couple days ago, literally they recommended approval six to zero. It slowed the decline. Now here's the thing that they didn't say, which they should have said, what are the things that performed better? This doesn't make you better, it doesn't keep you the same, it slows the decline by 27%. That's it. It slows the decline by 27%. So what worked better in their trials? Number one, ketones alone worked better than this drug. Number two, extra virgin olive oil alone in a trial worked

better than this drug. Number three, what's called combined metabolic activators, four different things that include some carnitine, some nicotinamide, riboside, things like that. Again, supporting energetics. This is about energetics and inflammation. Those are the two big players.

Dr. Joseph Mercola:

I couldn't agree more.

Dr. Dale Bredesen:

And then of course the protocol we developed worked the best of anything and we've got people now over 10 years who have sustained their improvement. So yeah, I agree with you. It's sad that this drug has been recommended for approval.

Dr. Joseph Mercola:

So why don't we highlight some of the biggest points in your protocol, because that is what you're promoting, that's what you're teaching, and you've got a lot of clinicians who are actually implementing this protocol at this time. What would you perceive as some of the biggest points of the program and the protocol?

Dr. Dale Bredesen:

Yeah, this is a great point and we can talk about specific people and how much better they've gotten, et cetera. But yeah, so there are two, as I mentioned, two major players, it's supporting the energy and it's reducing the inflammation. You have an innate immune system that lives in three sites: your bone marrow, your endothelial cells, and your tissue macrophages, which in the brain are the microglia. So we want to drop down that innate response, very much like what happens with COVID, and we also want to increase your energetics. And so to do that, we have two different pieces.

The first piece is a core piece that everybody gets, the second piece is the specific, so this is a precision medicine approach. If you have a specific infection, then you've got to deal with that and so many people have undiagnosed chronic infections. They may have, for example, P gingivalis, which does work its way into your brain from your oral microbiome, or T denticola. Herpes simplex is another common one. HHV-6A is another common one. So the basics are diet, exercise, sleep, stress, brain training, detox, and some targeted supplements. Those are the basics. And you mentioned this before, what about things like KAATSU bands? And so what we're finding is that those are helpful and something that I find very helpful is EWOT, exercise with oxygen therapy.

Most of these people are not getting appropriate energetic support to the far reaches of their brains. And so some people like to use HBOT (hyperbaric oxygen therapy), I like EWOT just because you're getting the blood flow as well, and you're getting not such a non-physiological amount of oxygen. So I really, and we've had some tremendous results with people on this, so I really like that one. But getting people appropriate, plant-rich, mildly ketogenic diet. And you've talked a lot about linoleic acid and its problems, you want that plant-rich, mildly ketogenic diet with a good omega-3 to omega-6 ratio, a good polyunsaturated fats, monounsaturated of course, and low in saturated fats of course. And the usual, no dairy, no grains, and no simple carbs. That's the approach that has worked the best.

We call that KetoFlex 12/3 and I'm really appreciative. Nutrition For Longevity has now launched it. So it's really easy. People have said to me, "Oh, I can't get this." You can actually now get it from Nutrition For Longevity. Just go on KetoFlex, K-E-T-O-F-L-E-X123.com, you can get these direct to you, it's really easy. So there are a lot of things that are making it easier for people to get better outcomes.

Then the specifics, as I mentioned, are typically chronic infections that are often undiagnosed. Sleep apnea, by the way, another common one that comes out in people, so many people, as you know, about 80% of sleep apnea goes undiagnosed. It unquestionably contributes to cognitive decline. You reduce

your oxygenation, you reduce the energetics to your brain, you increase your adrenaline while you're sleeping, et cetera. And then toxins and the toxins have been inorganics, organics, and biotoxins, everything from air pollution, and thankfully it sounds like you guys are far enough south you didn't get a problem with the Canadian fire.

Dr. Joseph Mercola:

No, never did. It's interesting, the Canadian government actually had an order that smoke could not go across the border. It didn't have a COVID immunization, so it was stopped at the border, thankfully.

Dr. Dale Bredesen:

Crazy. Yeah, this has been very unfortunate. We've had the California fires in the past and now unfortunately the East Coast is suffering with this air pollution. It's unquestionably a contributor to cognitive decline. And you mentioned COVID and it was really interesting for me to see, you probably saw on the Apple newsfeed literally the last two days, almost identical to what you've been talking about in the last couple years, where they're showing what's come from Wuhan, they're showing the furin cleavage site, they're showing the gain of function, all the things that people have been suspicious about are now coming out in this report, which I thought was really enlightening. All the stuff that's been denied.

Dr. Joseph Mercola:

Yeah. I wrote a whole book on that, "The Truth About COVID." But since we last spoke, my thinking has evolved on quite a bit in my understanding of health and medicine. And it has evolved to the point where I come to disagree with your statements about polyunsaturated fats and saturated because I now believe, and so there's one and then-

Dr. Dale Bredesen:

I'd love to hear more.

Dr. Joseph Mercola:

Oh, yeah. So I don't believe there's such a good thing as a polyunsaturated fat. I mean you could have some, you can go up to 2%. I think the biological optimum is probably about 1%, even lower. I currently have, this is omega-6, omega-6 now. Omega-3 is a different deal, which I'm still seeking to get to the core of, but I'm unequivocally confident that omega-6 is, in fact I'm in the third round of peer review now for a review paper on this to Nutrients. Just spent the first four hours this morning writing a three-hour rebuttal to one of the reviewers. So I think it'll get published.

But the studies that were done to support that omega-6 is an essential fat were done by the Burrs, it was a husband and wife team in the '30s. And there's been subsequent studies that disprove that because the way they implemented the study is they gave them no fat, no fat. No fat is not a good approach. You need some fat, it caused some skin deficiencies. They were mice, the studies were mice, so it caused some problems with their tails, but they could easily be remediated with certain nutrients or even small amounts of omega-3. So it's questionable at best that omega-6 is essential and it's all a moot point anyway because unless you're getting a laboratory diet, it's literally physically impossible to eat food and not get any omega-6. In virtually every food, I mean even watermelon has omega-6. So it's impossible to not get it. So you're going to get it.

I personally get less than 1% omega-6. Why? Because I mean the shift, it occurred in late 1800s where they had the technical ability to process seed oils industrially and make them in large quantities and they're cheap as can be. They're a lot cheaper than using animal fats, which are full of important

micronutrients, vitamin A, vitamin K2, which are essential for health. So they're cheaper and they're being used and the levels of this type of fatty acid in their tissue are increased by about 25 times, 2,500%.

Dr. Dale Bredesen:

Wow.

Dr. Joseph Mercola:

Yeah. I mean you do that on any nutrient and it's going to be potentially problematic. But with the omega-6, polyunsaturated, the PUFAs, the other name for them, is particularly problematic because they get embedded in the cell membranes, and not just your cells but also your mitochondrial cell membrane, specifically the mitochondrial membrane, and cardiolipin, which is a really important fat that's the only place it is in your body is in the mitochondria and it's in some of the complexes.

So when you got this highly perishable fat that's literally a time bomb waiting to be ignited by iron, you just set up this whole problem of lipid peroxides, like 4-HNE and malondialdehyde and glyoxal, and a whole variety of others that just destroys the surrounding tissue. So there's a lot of studies, I sent you a few links to some of them that really note a strong correlation, I don't know if there's any causal studies been published, because it's just hard to run.

One of the rebuttals I did in my review paper was, [inaudible 00:17:56] he says, "Well, linoleic acid has to be good. 15% of it is in breast milk, so it's got to be safe." So it took me a few hours to find it, but there was a study done in 1959 that literally in three days increased the linoleic acid concentration in breast milk from 8% to 40% just by feeding them pure soy oil and corn oil. So what's in the breast milk isn't assigned to that, but this is the type of thinking that goes on in a lot of the scientists out there.

So anyway, let's address that thread, because there's a lot of other ways and ultimately I couldn't agree more, it boils down to getting those mitochondria churning up and being as efficient and making as much energy as possible. And we got to talk about NAD and nicotinamide riboside because I think there's a better solution.

Dr. Dale Bredesen:

Absolutely.

Dr. Joseph Mercola:

But let's finish this one up with linoleic acid because I was so looking forward to discussing this with you.

Dr. Dale Bredesen:

So let me ask you, where do you like to see the omega-6 to omega-3 ratio?

Dr. Joseph Mercola:

Well, I think I'm not a big fan of the ratio. I think PUFAs are problematic and you got to keep them low. So there is no amount of omega-3 that you can take to offset a 25% LA content in your tissues. It just isn't, you just have to get it down low. Adding additional omega-3s is going to make the problem worse because it's also perishable, it's actually more perishable than omega-6, but it's stored a little bit differently, so it's not as easily oxidized. But I think 2:1, personally that's what I'm doing, 2:1. So I have less than three 3 grams of omega-6 per day in my whole diet and I have about a gram and a half of omega-3.

Dr. Dale Bredesen:

Okay, that makes sense. Yeah. And we typically look the same thing, anywhere from 1:1 to 4:1. So 2:1's perfect, right in the middle. The thing I worry about is when people are less than 0.5:1, of course it's associated with increased bleeding. That can be an issue for some people. And then where do you like to see, or do you like to look at the omega-3 index?

Dr. Joseph Mercola:

I don't know that you need to see an index. I use Cronometer, I'm sure you're familiar with that software-

Dr. Dale Bredesen:

Yeah, sure. I like Cronometer. Yeah.

Dr. Joseph Mercola:

Yeah. So I just look at the ratio there and it's pretty good, assuming your data is entered properly. So I mean you can do it occasionally, I don't think it's a huge, but I was a little confused in that I've had my omega-3 index up to 12 or higher, but now I think probably mid-single digits is probably fine.

Dr. Dale Bredesen:

Yeah, we shoot for people to get to right around 10% or so. So yeah, we're in the same ballpark there. And I think this is what people are seeing is good for inflammation and minimizing that, good for-

Dr. Joseph Mercola:

But you've got to be careful on your omega-3s, and I've done some articles on this, because the bulk of them, the majority of the omega-3 supplements out there are just worthless. They're actually worse than worthless because they're synthetic, they're ethyl esters, they're not the triglyceride form. Most of them are pretty clean because of the extraction process, but it contributes to the problem because they're not natural ones and they may be better than nothing, but I think in some cases it might be worse. You got to get the real deal, like the pure high-quality cod liver oil or something, and certainly something that hasn't been low in heavy metals and also the natural, not the synthetic form.

Dr. Dale Bredesen:

Yeah, absolutely. And along those lines, do you like resolvins as well?

Dr. Joseph Mercola:

Oh yeah, resolvins and protectants, but you're not going to get those in most fish oil supplements at all.

Dr. Dale Bredesen:

Yeah, exactly.

Dr. Joseph Mercola:

You got to get some from natural sources like cod liver oil or seafood. They're in seafood. Yeah, resolvins and protectants are great. Yeah.

Dr. Dale Bredesen:

Yeah. Fantastic. So those are the sorts of things that we address. Exercises, we talked about with EWOT. Sleep, of course, is a huge area in and of itself and so many people are doing themselves a disservice.

Patient zero, the first person that we treated back in 2012 who reversed her cognitive decline beautifully, I just talked to her on the phone a couple of days ago. She's now over a decade on this, doing great continually. She's now in her late 70s, and one of her issues was poor sleep. And of course, one of the things that was addressed, and again as I said earlier, getting the appropriate oxygenation during sleep, getting at least an hour of deep sleep and at least an hour and a half of REM sleep, very helpful. And of course, Matthew Walker wrote a whole book about why we sleep, really excellent information and they continue to do first-rate research in this area. And then of course, stress-

Dr. Joseph Mercola:

On sleep, what is your observation in elderly individuals? Do you find that typically this deep sleep tends to decline quite dramatically?

Dr. Dale Bredesen:

Yes, it can. And the problem of course is that poor sleep gives you more amyloid. Again, it's just a marker, but it's a marker of things that aren't so good. And unfortunately, amyloid then gives you poorer sleep. So unfortunately, you just kind of go downhill-

Dr. Joseph Mercola:

It's a cycle. Yeah.

Dr. Dale Bredesen:

And unfortunately, yeah, and poor deep sleep is often associated with too much adrenergic tone. So calming things down, actually you have a nice sleep pill with some melatonin in it and several other nice things, which I just took a few nights ago. Very helpful. So thanks for putting that together. And I think all of us can do better with our sleep.

Again, I think all of us can do better with our cognition. So many people say, "Look, I don't have Alzheimer's yet." Well, okay, but if you're 40 or over, please get a cognoscopy. Please get checked to make sure. You can do blood tests, you can do some simple online screening. Look, if you already have symptoms, get an MRI with volumetrics, but if you're there for prevention, you don't need that. There's so much that people can do to have a better cognition on a day-to-day basis.

Dr. Joseph Mercola:

Well, I want to finish up the testing first, and I definitely want to come back to the linoleic acid because I still don't understand your position on it. But the testing, you had those new exciting tests about the unfolded proteins, it sounded like there was commercially available, but I'm wondering what the pricing on that is. And then a follow-up question to that would be that you so accurately identified that these stealth infections that people have could be huge issues, and if their viruses are somewhat problematic, but there's certain ways you can approach it. So what type of testing panel do you use to screen for those?

Dr. Dale Bredesen:

Yeah, great point. So yes, so the point of the ones that are commercially available, you mentioned that the ones that are unfolded protein related, so pTau-181 is commercially available and-

Dr. Joseph Mercola:

And that's not an unfolded protein?

Dr. Dale Bredesen:

Well pTau-181, there is a fold of this, yes. But the pTau itself is you're basically phosphorylating the tau, which pops it off the microtubules so that you now are declining. It's part of signaling, but you're absolutely right, it also gives you preons, so these things become preonic because they are unfortunately part of the amplification of the signal for pulling back. So that one's commercially available. And then also the 42 to 40 ratio is commercially available-

Dr. Joseph Mercola:

Are these like $1,000 a test or what?

Dr. Dale Bredesen:

Okay, so yeah, great point. The pTau one is a couple hundred bucks, that's not so bad. The 42 to 40 is several hundred from Quest, but right, is over 1,000 from the one called Precivity. And the reason Precivity has essentially shown that there is a relation between what you'll get on your amyloid PET scan and what you'll get from their blood test. And they include your age and they include your APOE ε4 status. Do you have no copy, single copy, double copy? That's a critical, critical piece. Everybody should know their APOE status. So that's absolutely part of the genetic part of the blood tests.

So you're right. And to be fair, I think they priced it too high. It's something like 1,200 bucks and their argument is, "Well, it's less than a PET scan." Well yeah, but there are multiple other blood tests that you can get now so that you don't necessarily need to do that. So that was critical.

It's critical to know all the usual hormones, all the usual toxins. We like to look at the urinary mycotoxins. We also look at the GPL, typically the organic toxins, as you know. And then of course you want to know your metals and you want to know your exposure to air pollution. These are all critical to understand. You want to get a look ultimately at this amazing network that is supporting your synaptic network. And you need to understand this, if you've got problems with biotoxins, they are basically reducing your network size, they're reducing your synaptic network. So we look at all those.

And now of course epigenetics and there is a group called True Diagnostic working with multiple universities. They've done a great job. They're doing epigenetics for the test, our upcoming clinical trial. They're looking at brain aging, they're looking at biological age, they're looking at all sorts of things, and they'll get more and more associations as time goes on. I think that that's going to ultimately be the way for us to diagnose other neurodegenerative diseases early on so that we can get some really exciting improvements.

Dr. Joseph Mercola:

So what is the panel used to screen for those viruses, though? Is there is a specific panel that has them all? Or do you have to know what they are individually and just click them all?

Dr. Dale Bredesen:

Yeah. So the panels we use, so there's one for all the herpes family members, and those are the ones most associated, as you know, with neuronal and with brain changes. So you're going to get HSV-1, HSV-2, HHV-6. Now there's not a good HHV-6 A versus B yet, that is coming, and that will be very helpful because it's HHV-6 A that is less common, but more associated with brain degeneration of Alzheimer's. Whereas HHV-6 B, very common, most of us have it and most of us are not going to have a problem with it during our lifetimes. And then of course, EBV (Epstein-Barr virus), and I know you're aware of the recent EBV association with multiple sclerosis. The question now is, how does that work? You take 1,000 people at random, 940 of them will be positive for EBV, but only one of them will develop MS.

It seems to be very important, but it is not sufficient. It's necessary but not sufficient to give you MS. There is a very interesting cross reaction between a molecule in the brain called GlialCAM and the EBNA1 antigen. So there's a cross reaction between those two that is driving multiple sclerosis. So again, better and better blood tests coming up for all of these things. And then you mentioned the infections. Yes, you also want to look at chlamydia pneumoniae, which is another one that's critical.

You also want to look at all of the tick-borne infections, and I can't tell you how many times we find out that someone has an undiagnosed, whether it's Borrelia, Bartonella, Babesia, Anaplasma, any of these things that are all critical for, again for driving the innate immune system. Very much, you mentioned COVID earlier, very much like that. The difference is, of course COVID does it quickly and Alzheimer's does it slowly, but they are both innate immune system mismatches with the adaptive system. You're not clearing the pathogen, so you've got this continued. In one case, you die from cytokine storm as you've indicated before. In the case of Alzheimer's, you die from cytokine drizzle. It's a long-term cytokine problem. So those are critical tests.

And then again, as I mentioned, inorganic, organic, and biotoxins are all important to test for. Richard Horowitz, I'm sure you know, the international expert on Lyme disease has had some very good results using Dapsone for treatment of these chronic infections and showing improvements in cognition. And there was a very interesting study using Dapsone for people that have leprosy, which is, as you know, where it's commonly used. The people that got Dapsone did much better in terms of their long-term cognition than the people who were treated but did not get Dapsone. So this has an anti-inflammatory effect as well as an antimicrobial effect and looks like a very good candidate for the future.

Dr. Joseph Mercola:

Yeah. Stealth infections are clearly an issue. So, let's route back to linoleic acid because in my view, it may not be correct, but my current belief system, it may be the biggest source of all of these elements you just mentioned with respect to driving the process of increasing inflammation, oxidative stress, of damaging the mitochondrial proteins, the electron transport chains, so you cannot produce ATP (adenosine triphosphate) efficiently because if you've essentially stacked it with tinder and you've ignited it and it's burned up because you've got high iron levels, it's just a prescription for disaster. I'm wondering, if you've looked at the literature, if you've assessed it, if it's an area you're integrating into your protocol or what's your current view on that?

Dr. Dale Bredesen:

Yeah, great point. And we should also talk basically very much related to what you just said, we should also talk about fructose and we should also talk about methylene blue. You mentioned the methylene blue in your email to me that-

Dr. Joseph Mercola:

I'm a big fan of methylene blue. We could definitely dive deep on that. That's the oldest drug in the modern world. Literally preceded aspirin by about almost 25 years.

Dr. Dale Bredesen:

Interesting, interesting. So as far as the omega-6 and linoleic acid, I agree with you, this is something that can be a problem. It is pro-inflammatory, this is why we, again we're trying to target the network to be most functional. And part of that is we like to see the omega-3 index somewhere, 10% or so. And we'd like to see the [omega] 6:3 ratio being 1, up to 4:1, but no higher. And as you know, the American on average is about 15:1 or so, because we tend to get so much of that omega-6. I think people are beginning to come around and realize that this is not such a good thing after all. So I do-

Dr. Joseph Mercola:

Well, the simple solution, without having to spend a long time counseling people, it's just the no. 1 rule is no processed foods. That's where it's all at. It's all in the processed foods, which is a challenge because this means you've got to make your own foods, but it will solve it. And that includes restaurants because a lot of people confuse, "Oh, if I go to a restaurant, then all bets are off because it's a restaurant. I don't have to worry about it." No, that's just as bad, if not worse.

Dr. Dale Bredesen:

Yeah. Yeah. So now do you tell your patients, "Okay, you can go to a restaurant once a month, once a year?" Do you have a threshold or do you just tell them no-

Dr. Joseph Mercola:

It depends. I have no threshold. It's individual. If I had my druthers, I basically avoid them like a plague or I bring my own food. Or there are foods that you can eat there, like most beef even if it's commercially grown and loaded with Roundup and CAFO beef and fed grains their whole life, it's still going to be relatively low in linolenic acid. So, that's a safe one. A lot of seafood is, unless it was farmed. Vegetables, white rice. I mean there are things you can eat there that won't be a problem, but any salad dressing, any sauce, they're all made with seed oils.

Dr. Dale Bredesen:

Seed oil. Yeah.

Dr. Joseph Mercola:

Just got to be careful. The caution or the recommendation I make to friends if I go out with them occasionally, and I'm typically either I bring my own food or I don't eat at a restaurant.

Dr. Dale Bredesen:

Wow.

Dr. Joseph Mercola:

I tell the server that, "Listen," I show him my phone. I say, "I've got 911 on speed dial out here. My friend is deathly allergic to seed oils. If he gets any, you do not want the ambulance here because it's a bad thing. You got to go back there and talk to the chef or the cook that he cannot even see. It has to be butter. Has to be butter." It takes a little extra effort, but you can usually get it because they're not going to put butter in.

Or if you're having breakfast in a buffet, or making an omelet for you, I guarantee you, unless you go, they're not going to be using butter to make your omelet, they're going to using canola oil or whatever, some seed oil. So you can just tell them to use butter and look at it and make sure they're using it. There are things you can do, but you've got to pay attention to the details I think.

Dr. Dale Bredesen:

Yeah, that's such a good point. I wanted to talk a little bit about fructose because the work of Rick Johnson, and I suspect you probably talked to Rick-

Dr. Joseph Mercola:

Oh, Rick's been in my house before.

Dr. Dale Bredesen:

Oh, fantastic. Good. Yeah, so he's a professor at University of Colorado, just published a wonderful paper about two months ago, and actually Dave Perlmutter and I are both co-authors on that paper, but it's really the long-term research of Rick Johnson and what he's shown beautifully, you talked about the mitochondrial function, you're talking about damage to mitochondria, he's talking about a change in signal. So they're both important. As he points out, when you get that fructose, your body is literally responding to it saying, "Winter is coming. We are going to store fat and we're going to turn down your ATP by about 15%."

Well, when you're right on the ragged edge of getting enough energetics, then turning down your ATP by 15% is the last thing you want and is associated with cognitive decline. And I thought one of the things that was really striking, Rick put together a whole table looking at all the relationships, changes in PET scans, changes in blood biomarkers. In each of these cases, what happens with fructose is the same thing what happens in Alzheimer's disease. So again, it comes back to the critical nature of the energetics, whether you're turning them down by taking too much fructose and high fructose corn syrup, which is not to say, you can't eat some fruit, it just means you don't want to have massive amounts of fructose.

Dr. Joseph Mercola:

No, I was going to bring that up because I actually should get Rick back on to have this discussion with him because my views have changed quite dramatically. There's a world of difference between fruit and high fructose corn syrup.

Dr. Dale Bredesen:

Absolutely.

Dr. Joseph Mercola:

Because fruit, or fructose in the form of fruit, and just to let you know, I'm not low carb anymore. In fact, I eat about 500 grams of carbohydrates, mostly ripe fruit. So fructose from fruit actually activates pyruvate dehydrogenase, which as you know, you have to have that enzyme active if you ever hope to have glucose metabolized and broken down to pyruvate and have that pyruvate metabolized further to CoA, so it goes into the mitochondria to be burned efficiently as fuel. If you don't activate that, if it's shut down, you've got a problem and it goes down and you get the Warburg effect, you get production of lactic acid and the glucose seeps out because there's just too much of it. It's not being used.

The other point of contention I have on it, because I've studied this too, I know Rick's big into hibernation and torpor, but my understanding now is that really what causes that is the polyunsaturated fats. That's what causes torpor. And that, in addition to some of the inflammation that can happen when you have fructose from high fructose corn syrup, because it may be metabolized in a way that there's still there some filtered long chain starches that aren't broken down in your upper intestinal tract. They make it to your intestine. As you know, we've got 10:1 bacteria more than we have cells in our body, and if you have a higher percentage of gram-negatives, those are going to multiply and die eventually and the gram-negatives have the endotoxin cell wall, which contributes to increased serotonin and inflammation, leaky gut, potentially sepsis. It's a mess.

That's why you have to differentiate between high fructose corn syrup, or processed foods, and real fructose from fruit. I remember the last conversation I had with Rick, he was not opposed, in fact he was somewhat surprised, I think would be my memory of it, that fructose from fruit didn't seem to cause this.

Dr. Dale Bredesen:

Yes. And it makes perfect sense. Well look, the interesting thing to me is we are frugivore, we are descended from frugivores. So if you look at all the things, yeah, that was the thing that was driving the

simians that we descended from. The problem we have today, of course, is that our fruit has been bred to have a much higher sugar content. That's the one issue. But the good news is, of course, it retains the wonderful fiber and, as you pointed out, it doesn't give you that effect that high fructose corn syrup and processed foods does give you.

Dr. Joseph Mercola:

Yeah. And the other issue though, again, are you familiar with the Randle Cycle?

Dr. Dale Bredesen:

The Randle Cycle? No, tell me about the Randle Cycle.

Dr. Joseph Mercola:

Okay. The Randle Cycle, it's a metabolic switch and essentially it is just like a switch on a railroad track so that when you've got the fuel coming down, you've got fat and carbs, those are your only fuels, you can burn protein but that's beyond foolish to do that, so it's either fat or carbs. And how is your cell going to decide which one to burn? Well, it's the Randle Cycle and there's a threshold of fat. And it depends on how metabolically healthy you are, but it's about 30% to 35% as a cutoff point, so if you have more than that as fat, that switch kind of shifts it over to fat metabolism so that you're burning fat in your mitochondria rather than the glucose. The glucose gets shuttled down in glycolysis and then the excess goes out into your blood.

So if you have a lot of fruit and you're having a lot of fat, that's not a good idea because that can lead to diabetes too. So you've got to be careful with that throttle switch. And you make sure that if you're obese or you're diabetic, that threshold, that Randle Cycle might go down to 15%, 20%, not 30%. So to keep your mitochondria open to the glucose so it can come in, and then there's this other thing called, I don't know if we have time to go into it, but it's called reductive stress, which have you heard of that term before? Probably not.

Dr. Dale Bredesen:

Reductive stress.

Dr. Joseph Mercola:

Reductive, not oxidative stress. It's actually what causes oxidation.

Dr. Dale Bredesen:

Oh, I see what you're talking about. So essentially the opposite of oxidative stress?

Dr. Joseph Mercola:

Yeah, yeah. But where does it happen? It happens in the mitochondria when you have a backward flow of electrons from the complexes. And shockingly, this is at a foundational level, what the heck's going wrong with the polyunsaturated fats because you've got the polys, the linoleic acid embedded in the inner mitochondrial membrane and the cardiolipin and the complexes and if they're damaged, it shuts down those complexes and you get the backward electron flow through the complex, electron transport chain. And normally, if it's going forward like it's supposed to in an ideal world and if you're optimally healthy, the amount of reactive oxygen as a species that's generated, which we all know is a big thing, 0.1%, 99.9% efficient.

Dr. Dale Bredesen:

Yeah. Incredible.

Dr. Joseph Mercola:

Hardly any of us do that because we're full of the linoleic acid. So you get this reverse electron flow, which that's why methylene blue is so helpful because it can help stop that. But if you go forward, it's 0.1%. If you go the other way with reductive stress, it's 3% to 4% reactive oxygen species, 30 to 40 times more reactive oxygen species just by backing it up, which is what we've done with the modern dye. We just loaded the mitochondria with linoleic acid, just making it a recipe for disaster and radically increasing, and you get into this cycling effect because you get more oxidative damage, you damage more linoleic acid in the mitochondria membrane, and it just gets worse and worse and worse.

Dr. Dale Bredesen:

Yeah, very interesting. And so obviously you have a big interest in methylene blue.

Dr. Joseph Mercola:

Oh, I do. Oh, man. That is a profoundly serious understatement.

Dr. Dale Bredesen:

Interesting. And do you like it for Parkinson's or do you like it for Alzheimer's? Or-

Dr. Joseph Mercola:

I just like it for anyone who wants to improve their health and reverse degenerative disease, because it fundamentally is one of the key things to helping reduce reductive stress. Methylene blue will facilitate electron transfer forward in the mitochondria, even though the complexes are damaged. And the other thing is NAD, which I'm a big ... I don't like the typical precursors. I think they took NMN off the market because David Sinclair's company made, I think it's Metros or something made a drug-like, and had the FDA, I think it's pulled off as far as I know. So the only one left is really nicotinamide riboside, or NR.

Dr. Dale Bredesen:

Yeah.

Dr. Joseph Mercola:

But do you know what the best way to increase niacinamide is? I mean, or I said it, increase NAD?

Dr. Dale Bredesen:

NAD. No. So what is the way you like the best?

Dr. Joseph Mercola:

Well, this is pretty, it's not just me. I'm in the process of writing a bunch of articles on it, and the studies are really profound. It's simple. And you can buy a year's worth for ... A month's worth is under a dollar essentially.

Dr. Dale Bredesen:

Wow.

Dr. Joseph Mercola:

Instead of nicotinamide riboside which is over 100. So it's niacinamide, simple vitamin B3, not niacin, but niacinamide, taken in very tiny doses, like 50 milligrams because more will work, I used to think it was a problem because it inhibited the sirtuin and the sirtuins, as you know, David Sinclair promoted them as these massive longevity proteins that are so important to your health, but it turns out they're not what he's stacked them up to be and they could be problematic. So high doses of niacin impairing the sirtuins might actually be a good thing, but regardless, you just need niacinamide, about 50 milligrams three times a day.

Now, it only comes as a 500 milligram tablet commercially. We're in the process of making a 50 that should be out pretty soon.

Dr. Dale Bredesen:

Nice.

Dr. Joseph Mercola:

Fifty milligrams, but it's still cheap as can be and it will increase your NAD levels. And NAD+ is oxidized, right? So it's not reduced.

Dr. Dale Bredesen:

Right. Of course.

Dr. Joseph Mercola:

So it allows and facilitates the transfer of electrons forward in the electron transport chain. And methylene blue is also an oxidant, so it would ... So there's two ways, niacinamide actually fuels NAMPT, which is the rate-limiting enzyme for NAD+. And so you're making more endogenous NAD+, but once it's reduced, it goes to NADH. And when you have methylene blue, it goes in there and it oxidizes the NADH and turns that to NAD+. So that NAD+/NAD ratio is like that is the redox fuel, or not fuel, but meter, signal for your body because then there's a lot of others, like lactate to pyruvate and others.

But you want to get that NAD+ up so much, and it's not for longevity proteins, it's for making the complexes in your mitochondria work the way they were designed to, the way they figured it out in the early 1900s. I mean we all learn, everyone who takes biochemistry learns about NAD+, but they just don't understand how critical this thing is and how important it is to take a supplement. Do I think it's for all the neurodegenerative diseases you mentioned? Absolutely. For anyone else, cardiovascular disease, cancer, dementia, diabetes, obesity.

Dr. Dale Bredesen:

All right. Now related, one of the other things we see in these patients very commonly, the ones that have been exposed to mycotoxins or other toxins is low glutathione levels. So what is your favorite approach in terms of-

Dr. Joseph Mercola:

Well, I'm not a big fan of taking glutathione, I know people use it IV or sublingually, taking it away like liposomal glutathione could also work. And certainly some people benefit from increased levels, there's no question. But glutathione is reduced.

Dr. Dale Bredesen:

Reduced. Yeah.

Dr. Joseph Mercola:

And my understanding is you need the oxidized form to really make it work. So if you got a lot of methylene blue on, that could oxidize it back, but to make the actual molecule, you need cysteine and glycine. So cysteine you could take as NAC and glycine. Oh my gosh. The research on that. I mean you're probably aware of it, it's just crazy. It's so good. But it turns out there's a better way than getting a synthetic amino acid glycine than taking glycine. You know what that would be?

Dr. Dale Bredesen:

Nose to tail?

Dr. Joseph Mercola:

Nose to tail would be the ultimate, yes. Hard to do. Almost no one's going to do it. The other way is you could take what you would get in nose to tail, not including the muscle meat, which would be the connective tissue, which is about one-third of one-half of our protein in our body is collagen from connective tissue. So if you eat collagen or gelatin, you can get that connective tissue and you don't have to eat nose to tail. But that's about 30% of collagen or gelatin is glycine, plus it has other amino acids that are low that you don't need, like methionine and cysteine, tryptophan. There are problems when you get them in large amounts.

I know some people say, "Tryptophan, isn't it a precursor for serotonin?" Well, serotonin is a big problem, it's the happy neurotransmitter, but there's a lot of research that it causes a lot of problems like fibrosis and inflammation in pairs, metabolism shuts down your metabolism. So in large quantities, and you make it in your gut. Most of it's in your gut, although it does transfer up to your brain. But it's one of the problems that happen when you get exposed to a lot of these resistance starches that you eat and don't get digested and then fueled up in the gut, and then you get that bacteria converted.

Dr. Dale Bredesen:

And then two final things on the methylene blue you were talking about. Number one, LMTM (leuco-methylthioninium bis-hydromethanesulfonate) versus the methylene blue itself.

Dr. Joseph Mercola:

Yes.

Dr. Dale Bredesen:

I know there are issues there. And then number two, the dosage you like, you looking at eight to 10? What's sort of-

Dr. Joseph Mercola:

Yeah. Yeah. Excellent questions. LMTM for those who aren't familiar with, that's the reduced form of methylene blue, it's actually clear. That's what happens when methylene blue, because it is a dye, if it's blue, its oxidized and it will stain. If you're playing with this, I mean just the tiniest speck will stain your counter, guaranteed. If you play with this, you do it in the sink, a stainless steel sink.

And I know the trials with the dementia were done with the reduced form, and I don't think they got great results because at least the one trial I sent you was they used an 8 to 10 milligram and a 150 to 250, and there was no difference, which suggests that the 8 to 10 milligram is all you need. For some people, they might need a little more, maybe as high as 50, but 100, 250 milligrams is way over the top and about somewhere between 30 and 50 milligrams, your urine will turn blue. And some people suggest that the lowest dose that your urine turns blue is the healthier you are essentially, because you don't need the

methylene blue to go in and reduce things or oxidize things that are reduced. And one of the things I learned about this too is that with the reductive stress, I'm sure you're familiar with grounding, right?

Dr. Dale Bredesen:

Sure. Yeah, of course.

Dr. Joseph Mercola:

I was always confused on why grounding worked, because typically you're thinking, okay, if you shuffle your feet on a rug, you build up these electrons in your body and you touch a door handle and the spark, you're discharging those electrons. I didn't think how that worked, I thought it was supposed to reduce oxidative stress. Well, it does and that's exactly what it does, because usually the problem is you have too many electrons and that's what our food is. Our food is a source of electrons, right? Carbs and it passes electrons through, passes them ultimately to oxygen, making metabolic water and carbon dioxide, but it's electrons, which are reductants.

Dr. Dale Bredesen:

Redox. Yeah, redox chemistry.

Dr. Joseph Mercola:

Yeah. Yeah. So it's so key. And it's pretty basic chemistry. It sounds confusing, but it really isn't when you study it. But yeah, so grounding works too. And grounding can help make the mitochondria work better, because I never knew how it worked, but it makes the mitochondria work because it reduces reductive stress. It discharges those electrons into the earth because it's grounded, right?

Dr. Dale Bredesen:

Absolutely. Very interesting. Very interesting.

Dr. Joseph Mercola:

So, yeah, I think the dose is about 10 milligrams for most people. It seems our environment today, to me that's a two ... It's just almost, I mean they're so cheap. I mean integrating those both together would cost $1 or $2 a month. There's virtually very few people who couldn't afford that. It's like universally available, affordable, and almost no side effects. I mean one side effect, methylene blue, potentially if you took a higher dose, it's a monoamine oxidase A inhibitor, so it could potentially, that's the enzyme that's used to degrade serotonin. So if you were on an SSRI and you had high serotonin levels, it couldn't raise your serotonin, you can get serotonin syndrome, which would not be good. So if you're on SSRI, potentially a problem, although I've seen many people taking SSRIs, at small doses it seems to work, even as high as 50 milligrams a day without any problems, but it's still potentially an issue.

Dr. Dale Bredesen:

Absolutely. So let me mention one other thing, because the common thing is, "So-and-so in my family has a problem with neurodegeneration, what do I do?" And there hasn't been any institute in the country or in the world-

Dr. Joseph Mercola:

Until yours.

Dr. Dale Bredesen:

So, yeah, so we're just starting. I'm very excited, this should be opening later this year or early next year. This is at Pacific Neuroscience Institute. This will be the Precision-

Dr. Joseph Mercola:

Where is it? Where is that?

Dr. Dale Bredesen:

... Medicine Program. That's in Santa Monica, California, so right there in Western LA. And this will be a site, and we're doing this with Dr. David Merrill, Dr. Dan Kelly, the whole group at PNI. And the idea is to open this as a first place for Precision Medicine Program, so for people who have dry macular degeneration, for people who have PSP, CBD, Lewy body disease, Alzheimer's, et cetera. Again, as you said earlier, we encourage everyone, please come in for prevention or earliest treatment.

As you know, when you get Alzheimer's, you go through four stages. You go through a presymptomatic phase, you go through subjective cognitive impairment that lasts on average 10 years. These areas, pretty much 100% effective. We can prevent, we can reverse virtually every time people are an SCI. MCI is the next, it's too bad it's called mild cognitive impairment. It's like telling someone they have mildly metastatic cancer. It's a relatively late stage of Alzheimer's disease. We still, in our trial, had 84% of those people improve.

Then the final stage is dementia. And we still see some people with proof of dementia. But the farther you go, the harder-

Dr. Joseph Mercola:

The harder it is.

Dr. Dale Bredesen:

And the tougher it is to get them all the way back. So we encourage everyone, please come in early.

Dr. Joseph Mercola:

What stage do you think Biden's in?

Dr. Dale Bredesen:

That's quite a loaded question. Let me suggest that that brings up a really critical question, which is, should we have a law, we already tell people you have to be at least 35 to run for president in the United States, you can't be 25. So why is there no upper limit? I would propose an upper limit of 75, 35 to 75. Not to say that there aren't a lot of smart 80-year olds and even 90-year olds and some 100-year olds. The other option is do testing and make sure someone's sharp at 80, whatever it is. So-

Dr. Joseph Mercola:

The had Trump, Trump took cognitive tests, but Biden didn't.

Dr. Dale Bredesen:

Yeah. Well, so we'll have likely next November, we will have the two oldest candidates ever, and one will be over 80 already, the other one will become 80 while he's president if he gets elected. I do think that's something that has to be taken into account by all, and maybe you're right. Maybe the best way is just do appropriate testing before the person can run-

Dr. Joseph Mercola:

Well, in my mind it's somewhat discriminatory unless you do that approach because you could-

Dr. Dale Bredesen:

It is discriminatory.

Dr. Joseph Mercola:

I mean literally you could be more fit mentally by 200% to 300% than someone younger because it really depends on what you've been doing and integrating all these recommendations. And if you're doing it and there's nothing wrong, then you just have to arbitrarily, because of an age, because that's the age that most people are doing these things and then invariably come down with neurodegenerative challenges.

Dr. Dale Bredesen:

Yeah. I think this is a political issue and a biological and medical issue.

Dr. Joseph Mercola:

[inaudible 00:56:40] are going to be speaking at a dental event in Orlando on my part of the world in September.

Dr. Dale Bredesen:

Yep. Looking forward to it. Collaborative viewers. Yeah. And I think that you know this very well, the dentists have done a fantastic job with looking at oral systemic specialists to say, "Look, this is related to your mercury level. This is related to your oral microbiome, which affects cancer, which affects inflammation, which affects cognition, which affects atherosclerosis. It's incredible how important this is." And again, there are toxicity issues and there are also airway issues. One of the most common is poor support so that now people are going to sleep, they've got more sleep apnea, obstructive sleep apnea. These all are critical things that should be dealt with and we need more interaction between people who are interested in cognition and neurodegeneration and even internal medicine and those who are interested in oral health.

Dr. Joseph Mercola:

Do you ever recommend using paper tape over your mouth at night to make sure that you're only breathing through your nose and not breathing through your mouth?

Dr. Dale Bredesen:

Only for those who have no trouble breathing through their nose. For those people, I have no problem. But for many people, they don't breathe well through their nose and so taping their mouth shut is a real problem.

Dr. Joseph Mercola:

Make it worse. Make it worse.

Dr. Dale Bredesen:

Exactly. So I think it's critical to find out, you can actually measure airway size and it's critical to have a sleep study. Look, wearables, as you know, wearables are going to change the world. We can look at so many things now. We can look at our HRV and we can look at our blood pressure and we can look at our various sleep phases-

Dr. Joseph Mercola:

They're objective. They're objective.

Dr. Dale Bredesen:

Yeah. So I think these are going to be fantastic and they'll tell you. So I think it's important to track, and I'm sure you track your oxygenation while you're sleeping. There's a beautiful paper from a couple years ago just looking at the average SPO2 at night correlates beautifully with the average size of your hippocampus and other nuclei in the brain. So, your oxygen's going down at night, okay, then your brain size is going down. So that's critical to get that up.

Dr. Joseph Mercola:

Unless you're doing it intentionally actually, because one of my practices, for [inaudible 00:58:55] is I have an apparatus that essentially replicates different altitudes and it's done through a mask. I can do partial pressures of oxygen below 10% if I wanted to, but I usually hang out around 13.5%, 14%. But I'm going to set it up so I can sleep at night with this mask on and probably go down really slowly, maybe, instead of 20% oxygen, maybe 19% or 18.5%, because there's so much good literature that those who live at altitude, over time, they do so much better and it appears to increase CO2 concentrations.

Dr. Dale Bredesen:

That is really interesting. So yeah, it's going to be interesting to see how you balance it because you don't want to go too low for too long-

Dr. Joseph Mercola:

Right, right. You do not want to go too low, right.

Dr. Dale Bredesen:

But a lot of people-

Dr. Joseph Mercola:

Has to be done slowly.

Dr. Dale Bredesen:

... like to cycle. Now do you cycle normally? That's another thing, of course, at LiveO2-

Dr. Joseph Mercola:

Oh yeah, yeah.

Dr. Dale Bredesen:

... which have done that nicely.

Dr. Joseph Mercola:

Yeah. This is a little more precise. It's a medical grade unit where LiveO2 is just a run of the mill concentrator and after a few hundred hours those regular concentrators, they start producing toxins like aluminum and things. It's a real problem. So this is medical grade and yeah, I go down to 13.5% for five minutes and it goes up to 34% oxygen for a minute. And you just cycle in it out. And I get my PO2 down to high 70s.

Dr. Dale Bredesen:

Wow.

Dr. Joseph Mercola:

Yeah. But it's a cycle, it goes in and out and you can stimulate HIF-1-alpha and you get all these great benefits. But I want to also do the nighttime sleeping to simulate altitude training.

Dr. Dale Bredesen:

Interesting. So let me also ask you, you and I had a discussion several years ago about how important ketones are, and certainly the work from Professor Stephen Cunnane shows just giving exogenous ketones to people with MCI does improve their cognition. It's part of energetics, but as you pointed out, you want to cycle out of this and I think you told me at the time, at that time you were recommending twice per week to cycle out. What's your current thinking about this? I know you're now more of a frugivore, so you maybe-

Dr. Joseph Mercola:

Yeah. I totally evolved out of that and many, many people, you know anecdotally and probably hundreds, thousands, tens of thousands of people that you know personally that have benefited from this approach, but I think it's problematic. And there's actually a study published last month. No, yeah, this is last month, it was in May of 2023 that looked at, I think it wasn't prospective, I think it was epidemiological, so it was correlation, it wasn't causation, but they looked at low carb/high fat, high fat/low carb, and they impacted mortality rates.

And I had shifted before I saw this study, but it was confirmational bias that I found it. But the low carb/high fat had an increased mortality rate of 30% and the high carb/low fat had a decreased mortality at 30%. So I'm just concerned about this. And here's one of the things is really what catalyzed it, and I didn't understand this and perhaps you do or don't, I don't know, but I didn't, I was clueless, and I'm sure you've seen it. After the first few days of going on a fast or low carb, I mean you'll improve. Your glucose drops, everything gets better. But then, after a few days, usually after your glycogen stores run out, your glucose comes back up and you're eating no glucose, none, zero carbs.

So where does the glucose come from? It comes from cortisol. So you're raising cortisol levels. That cortisol, how does it raise your glucose? It's a gluconeogenic hormone. It raises glucose. That's its primary function. And it does this by stripping your brain, your bones, and your muscles of protein, amino acids, it shreds them, gone and it increases inflammation. Is it great to have this? Absolutely. You'd be dead without it. Thank God this system exists. But if you do it continuously, you are asking for trouble. And I think that's what contributed to that observation that they found on that study.

It's really problematic. So I don't recommend it at all now personally, although everyone has to make that choice and decision for themselves, for sure, but personally I wouldn't do it. And in fact, what's improved my sleep dramatically is I take a teaspoon of honey and a teaspoon of gelatin before I go to bed, and my deep sleep has improved pretty significantly.

Dr. Dale Bredesen:

Very interesting. All right, very interesting. Well clearly-

Dr. Joseph Mercola:

So well-digested food, you're not eating a burger or something that you have to, that pretty much breaks down the amino acids and the sugar quickly.

Dr. Dale Bredesen:

Very interesting. I mean the problem we run into with people with cognitive decline, they have lost both. So they're no longer burning glucose appropriately. They've got insulin resistance. They've lost their ability to make and utilize ketones because their insulin is high. They got nothing, and unfortunately are low in their energetics. So we need to restore both of those. And you've kind of done it in a very different way than we have, but the key is to restore both, the ability-

Dr. Joseph Mercola:

Yeah. You need to be metabolically flexible, for sure.

Dr. Dale Bredesen:

Exactly.

Dr. Joseph Mercola:

Yeah. You've got to be able to have that capacity to seamlessly switch between burning fat, which you need, you definitely need it. When I do my KAATSU blood flow restriction training, I go anaerobic and the glycogen is gone. You got to be able to switch to fats, but you don't want to do that continuously for long periods of time, you want to do it for short periods of time. Cycling, I think, is the key. Cycling in and out where you're not doing it for long term.

Dr. Dale Bredesen:

Interesting. Very interesting.

Dr. Joseph Mercola:

Yeah. So, I mean we both got into this because we love helping people, I'm confident of that. But the other part of this is it's just like a big puzzle. If you're truly committed to, as I believe you are, truly committed to helping people and looking at the truth, not being persuaded or influenced by corporate interest and following this path and being afraid to say the truth because of losing your job or your hospital privileges. So when you have that, life is such a joy because it's just this journey to discover the truth.

Dr. Dale Bredesen:

Yeah, yeah. I mean best outcomes, that's the key. And getting emails and getting notes and things that say, "Look, this person had no hope and is now doing very well." There's nothing better than that.

Dr. Joseph Mercola:

Yeah, because you are such an anomaly in the world of dementia treatment. There's virtually no one or group that is holding the hope that you ... I mean before you arrived, this was irreversible and the only solution was to take some drug which is going to make you worse.

Dr. Dale Bredesen:

Exactly. Yeah. It's been really sad to see, as you know, the antibodies have been associated with more brain atrophy, the standard cholinergic approach has been, unfortunately using things like Aricept and Namenda has been associated — both Aricept and Namenda have been associated with a poorer outcome just five years down the road. So you're right, it's been a really tough situation. And of course, with the antibodies that are getting approved, there's more brain hemorrhage, there's more brain swelling, there

have been multiple deaths. They're astronomically expensive. It's just an absolute mess, so I think we need to do better.

Dr. Joseph Mercola:

Yeah. And kudos to you for moving the field in that direction. How have your colleagues responded to your approach? Been getting a lot of criticisms? Is there conflicts? Have you lost friends?

Dr. Dale Bredesen:

Oh yeah. No, I've lost a lot of friends. And many of my old colleagues literally will not talk to me because they're holding onto this hope that we're get a drug, we're going to get a drug. It's one drug is going to do it. And I think, I hope one drug does it. That would be great-

Dr. Joseph Mercola:

We both know it's not going to happen. Just like a drug to treat obesity, it's not going to happen. We could do it-

Dr. Dale Bredesen:

Well, I think the fact that this is a network, that's the key. This is a network. You got to address all the different pieces. And of course, as you mentioned, metabolism is a huge issue.

Dr. Joseph Mercola:

Oh, it's the biggest part of the puzzle, I think for almost every disease. Once you crack that nut in a kernel, everything flows and the rest of it's just fine tuning and support and synergistic support as you're doing in your protocol is all these little pillars you've got, you address one of them, they all add up and they build this strong synergy that produces pretty dramatic results.

Dr. Dale Bredesen:

Absolutely. Yeah. One last, what's your take on stem cells? So we've got to remove the problem that's causing the degeneration-

Dr. Joseph Mercola:

Yeah, yeah, yeah. I think it has a lot of potential.

Dr. Dale Bredesen:

... [inaudible 01:07:58], but ultimately we got to rebuild the synapsis. So what is your take on stem cell approaches for that third piece?

Dr. Joseph Mercola:

Not in favor of most stem cells, but the concept I'm in favor of. There's a guy in your neck of the woods, Todd Ovokaitys, I'm unsure if you've encountered him, but-

Dr. Dale Bredesen:

Sure, yeah, I know Todd.

Dr. Joseph Mercola:

Okay. Yeah. So I'm a favorite of Todd's approach. And once you learned of Todd's work, it's almost a joke every other type of stem cell approach. I would never do it. I mean I would only do Todd's and I actually, I'm one of Todd's licensed stem cell — I don't treat other people, but I treat myself and friends with that.

Dr. Dale Bredesen:

Wow. Interesting.

Dr. Joseph Mercola:

So I've got one of the units in my house. So I'm a big believer of that. It's something like, for those who are not familiar with it, it's something like PRP, plasma-rich platelets, platelet-rich plasma, sorry. And essentially spin the blood down, it's your own blood, it's not taking stem cells from somebody else, your stem cells, these are these primitive sleeping stem cells and his process extracts them in a centrifuge and inject them back into your body after they've been activated with a laser, so waking them up. So I like that a lot. And he's got some pretty darn good results. So-

Dr. Dale Bredesen:

Interesting.

Dr. Joseph Mercola:

Yeah.

Dr. Dale Bredesen:

Well we're all interested in the same thing; best outcomes, how do we-

Dr. Joseph Mercola:

Absolutely. Absolutely.

Dr. Dale Bredesen:

... we have to do to get the best outcomes. We've had people go from MoCA (Montreal Cognitive Assessment) scores of 18 to 30, which is fantastic, from demented to normal. We've had people go from zero to 9. We've never seen anyone yet be able to go from zero MoCA, which is end-stage Alzheimer's to perfect 30. I look forward to that someday, when we understand this-

Dr. Joseph Mercola:

What's the best you've seen? What's the best you've seen?

Dr. Dale Bredesen:

18 to 30. So people go-

Dr. Joseph Mercola:

So once you're below 18, it's a real problem.

Dr. Dale Bredesen:

Well, we've seen people go from 16 to 25 and do absolutely great. We've seen people go from 15 to 27 even and do absolutely great.

Dr. Joseph Mercola:

That's pretty good. So what's the threshold, if you go below 10 it's kind of hard to reverse it?

Dr. Dale Bredesen:

So everybody-

Dr. Joseph Mercola:

Because it's like a cancer, once the cancer's too far gone, you can't reverse it. It's just gone.

Dr. Dale Bredesen:

So here's the thing, this is what's really interesting. A guy wrote me a nasty note a couple years ago and he said, "How dare you tell people that if they're too far along, they shouldn't get on this protocol?" He said, "My wife had a MoCA score of zero. She's in a nursing home. We used the protocol that you developed, she only went up a little bit, but her symptoms were so much-"

Dr. Joseph Mercola:

That was significant. Yeah.

Dr. Dale Bredesen:

"She could dress herself, she could speak again, she could engage."

Dr. Joseph Mercola:

Good point.

Dr. Dale Bredesen:

So I don't say there's anything, but it is much harder below 16.

Dr. Joseph Mercola:

Okay. So 16 is the threshold.

Dr. Dale Bredesen:

We see that again and again and again. It's harder below 16.

Dr. Joseph Mercola:

So you're probably not going to get amazing improvement, but you could get partial improvement, which would be pretty significant for the lowest-

Dr. Dale Bredesen:

You can get some dramatic subjective improvements. And again, we've seen people like 15 to 27. It does happen, it's just that, just like with cancer, it is harder and harder and harder the longer you wait. Which is

why we encourage everyone, look, if everybody would come in in those first two phases, prevention or SCI, dementia would be a rare problem.

Dr. Joseph Mercola:

Yeah. Kudos to you for putting this together and really addressing the foundational disturbances that the body's experiencing by addressing the causes typically. You can activate the body's recovery and repair mechanisms, which are there. Our body wants to be healthy. A lot of doctors don't get this, it strives to be healthy, you just got to remove the impairments to that. And you're doing a great job with respect to neurodegenerative disease, so congratulations. All right. Well thanks a lot. Keep up the good work.

Dr. Dale Bredesen:

Stay safe and well.

Dr. Joseph Mercola:

All right, you too.