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How to Help Prevent and Treat Alzheimer's Disease

Analysis by Dr. Joseph Mercola Fact Checked | July 02, 2023

STORY AT-A-GLANCE

- In 2014, Dr. Dale Bredesen published a paper demonstrating healthy lifestyle choices could reverse Alzheimer's in 9 out of 10 patients. His team is now launching a new randomized, controlled trial at six sites. Biological aging, brain aging and epigenetics will be included in this trial, using newer blood tests that weren't available even a few years ago
- The glial fibrillary acidic protein (GFAP) test can be a valuable tool. This test basically looks at brain changes associated with astrocytosis. Astrocytes respond when there's a problem in the brain, so it can give you a heads-up that something is afoot up to 10 years before symptoms set in
- Supporting energy production and reducing inflammation in the brain are the two most important factors to prevent and treat Alzheimer's
- The entire family of herpes viruses is associated with changes in the brain and neurons. Left untreated, chronic infections put your innate immune system into overdrive. Alzheimer's is an innate immune system mismatch with the adaptive system. You're not clearing the pathogen, so you've got a continued onslaught of cytokines causing damage in your brain
- Valuable adjuncts that can help improve mitochondrial energy production include methylene blue, niacinamide, NAC and glycine

In this video, I interview repeat guest Dr. Dale Bredesen, a neurologist specializing in the treatment of Alzheimer's. In 2014, he published a paper[1] demonstrating the power of

lifestyle choices for the prevention and treatment of this tragic condition. By leveraging 36 healthy lifestyle parameters, he was able to reverse Alzheimer's in 9 out of 10 patients.

This included the use of exercise, ketogenic diet, optimizing vitamin D and other hormones, increasing sleep, meditation, detoxification and eliminating gluten and processed foods. It's been several years since we spoke last, so he's got quite a few updates to share.

Randomized Trial Launch

For starters, his team has published another proof-of-concept paper and are now launching a randomized, controlled trial at six sites: Hollywood, Florida; Nashville, Tennessee; Cleveland, Ohio; and Sacramento, Oakland and San Francisco in California.

Biological aging, brain aging and epigenetics will be assessed in this trial, using newer blood tests that weren't available even a few years ago, including phospho-tau 181, phospho-tau 217, A-beta 42 to 40 ratio, glial fibrillary acidic protein (GFAP) and neurofilament light polypeptide (NF-L).

> *"A couple of these are not commercially available yet, so we're doing these as research, but they will all become commercially available,"* Bredesen says. *"Currently, phospho-tau 181 is commercially available and so is the A-beta 42 to 40 ratio. So now, for the first time, you can get an idea, without necessarily having a PET scan, where you stand.*
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> *More importantly, you can follow it as you improve. Prevention is key, but also reversing cognitive decline, which we were the first to do ... We've seen it again and again, when you're doing the right things, when you're attacking the important drivers of the process, you see [reversal]."*

Valuable Tests

The GFAP test, while nonspecific, can be a valuable tool. This test basically looks at brain changes associated with astrocytosis. Astrocytes respond when there's a problem in the brain, so it can give you a heads-up that something is afoot up to 10 years before symptoms become apparent. "The good news is if it's normal, you're in pretty good shape. So you want to know that going forward," he says.

The phospho-tau 181 and phospho-tau 217 are specific tests for Alzheimer's changes related to the death of neurons. Genetic testing is also important to ascertain how many copies of the APOE ε4 gene you might have. "That's a critical piece," Bredesen says. "Everybody should know their APOE status." Hormone testing and testing for toxins, including mycotoxins and heavy metals, are also important.

Where There's Smoke There's Fire

According to conventional thought, elevated tau and beta-amyloid are causative factors in Alzheimer's, but Bredesen's research suggests otherwise. He explains:

> *"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 makes no sense. The key thing to know is that [tau and beta-amyloid] are responses and mediators. You've talked a lot about mitochondrial function, which is absolutely critical in this disease, but we know of many upstream contributors, and that's another update.*
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> *People have not known what's causing this disease, and it's often said there's nothing that prevents, reverses or delays it. Nothing could be further from the truth. We know there are many contributors, [including] anything that damages mitochondria [and] different infections.*
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> *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, that network is no longer sufficiently supported.

And, no surprise, it pulls back and that's why you see the tau. They are part of the mediators of making this effect enhanced. They amplify the problem. 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 but a terrible therapeutic target, and that's exactly what's coming out of the data.

Unfortunately, Lecanemab was just recommended by the panel for FDA approval. It slowed the decline. But here's the thing they didn't say, which they should have said, what are the things that performed better? Lecanemab doesn't make you better, it doesn't keep you the same, it slows the decline by 27%. That's it.

So what worked better in their trials? No. 1, ketones alone worked better than this drug. No. 2, extra virgin olive oil alone in a trial worked better than this drug. No. 3, combined metabolic activators — carnitine, nicotinamide, riboside, things like that. Again, supporting energetics. This is about energetics and inflammation. Those are the two big players.

And then of course, the protocol we developed worked the best of anything. We've got people now who have sustained their improvement for more than 10 years. So, it's sad that this drug has been recommended for approval."

Two Key Causative Factors That Must Be Addressed

According to Bredesen, supporting energy and reducing inflammation in the brain are the two most important factors to prevent and treat Alzheimer's. Basics that all of Bredesen's patients implement include:

Dietary intervention — Bredesen recommends a plant-rich, mildly ketogenic diet, with a good omega-3 to omega-6 ratio, no dairy, no grains and no simple carbs. "That's the approach that has worked the best," he says. "We call that KetoFLEX 12/3." Nutrition for Longevity now offers meal kits for the KetoFLEX 12/3 diet at KetoFlex123.com, to make it easier to follow.

In the interview, I counter some of Bredesen's dietary recommendations, as he still recommends polyunsaturated fats (PUFAs).

I'm convinced all omega-6 PUFAs need to be kept low, below 2% or even 1% of daily calories, for optimal health, and I strongly suspect people with dementia need to be even more cautious, as the PUFA linoleic acid (LA) appears to be the biggest dietary source of all the drivers of Alzheimer's, including inflammation, oxidative stress, mitochondrial dysfunction and dysfunction in electron transport chain such that you cannot efficiently produce ATP.

I've written extensively on the ins and outs of this, so for more information, listen to the interview and/or review "Linoleic Acid — The Most Destructive Ingredient in Your Diet."

I'm also not convinced that the omega-3 to omega-6 ratio is as helpful as commonly suggested since you cannot counter the damage caused by omega-6 fats simply by taking more omega-3. On top of that, most omega-3 supplements, primarily fish oil, are worthless because they're synthetic and rancid to boot, so making sure you're getting high-quality omega-3 is an essential factor.

Exercise — Bredesen is seeing particularly good results with KAATSU (blood flow restriction training) and exercise with oxygen therapy (EWOT).

Sleep optimization — Sleep apnea is a common problem that unquestionably contributes to cognitive decline, as it reduces oxygen to your brain and raises adrenaline while you're sleeping.

“Sleep is a huge area in and of itself,” Bredesen says. “Patient zero, the first person we treated back in 2012 who reversed her cognitive decline beautifully, she's now over a decade in on this, doing great continually. She's now in her late 70s.

One of her issues was poor sleep and, of course, one of the things that was addressed. Getting at least an hour of deep sleep and at least an hour and a half of REM sleep is very helpful ... Poor sleep gives you more amyloid. 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.”

Stress reduction

Brain training

Detox

Targeted supplements

The other part of Bredesen’s program is customized to each patient. Many have undiagnosed chronic infections, for example, that need to be addressed. Common ones include P. gingivalis and T. denticola, which work their way into your brain from your oral microbiome, herpes simplex and human betaherpesvirus 6A (HHV-6A).

The entire family of herpes viruses is associated with changes in the brain and neurons. HHV-6A in particular is associated with the brain degeneration seen in Alzheimer's. Chlamydia pneumoniae is also highly troublesome, as are all tick-borne infections, including Borrelia, Bartonella, Babesia and Anaplasma.

All these infections put your innate immune system into overdrive and need to be quenched. As noted by Bredesen, COVID-19 and Alzheimer’s are “both innate immune system mismatches with the adaptive system.” You're not clearing the pathogen, so you've got this continued onslaught of cytokines. In the case of COVID, you die from the acute cytokine storm, whereas in Alzheimer's, you die from cytokine drizzle. “It's a long-term cytokine problem,” Bredesen says.

High-Fructose Corn Syrup Down-Regulates ATP Production

Bredesen also highlights the importance of avoiding fructose. In March 2023, Dr. Richard Johnson, Bredesen, Dr. David Perlmutter and several other coauthors published a paper[2] on Alzheimer's disease as "a maladaptation of an evolutionary survival pathway mediated by intracerebral fructose and uric acid metabolism."

> *"It's really the long-term research of Rick Johnson. You talk about mitochondrial function, about damage to mitochondria. He's talking about a change in signal. 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%.'*
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> *Well, when you're right on the ragged edge of not getting enough energetics, then turning down your ATP by 15% is the last thing you want and is associated with cognitive decline.*
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> *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 that happens in Alzheimer's disease.*
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> *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."*

Fruit Versus High-Fructose Corn Syrup

Here too, my current views veer a bit. It's important to understand there is a world of difference between fructose from fruit and high-fructose corn syrup. I used to recommend limiting both sources, but I've recently changed my thinking on this, as fructose from fruit activates pyruvate dehydrogenase, which you need to metabolize

glucose from pyruvate to acetal-CoA in your mitochondria. If that enzyme is not activated, the glucose cannot be used for fuel.

The key to this riddle for me was the Randle Cycle, which basically acts as a metabolic switch. Your primary fuels are fats and carbs, and the Randle cycle determines how your cells decide which one to burn. When your diet is more than 30% to 35% fat, this switch shifts to fat metabolism, so that you're burning fat in your mitochondria rather than glucose. The glucose instead gets shuttled into glycolysis and any excess goes out into your blood.

So, eating a lot of fruit and a lot of fat at the same time is not a good idea. In essence, fructose by itself is not what's causing the problem. Rather it's eating too much fructose in combination with too much fat. If you increase your fresh fruit intake, you also need to lower your fat intake, or else the sugar can't be used for fuel.

Additionally, there are individual variations in metabolic flexibility, toxicity and microbiome that likely contribute to a person's ability to tolerate increased carbohydrates.

The other point of contention I have is that PUFAs also appear to induce torpor (decreased physiological activity marked by a reduced metabolic rate), much like high-fructose corn syrup does. So, I suspect ripe fruit is not going to be a major contributor to dementia. In a previous interview with Johnson, he also admitted being surprised that fructose from fruit did not have the same effects as high-fructose corn syrup. Bredesen replies:

> *"Yes. And it makes perfect sense. The interesting thing to me is we are frugivore (animals that thrive on raw fruits), we are descended from frugivores. The problem we have today, of course, is that our fruit has been bred to have a much higher sugar content. That's the issue. But the good news is, 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 give you."*

Methylene Blue, Niacinamide, NAC and Glycine

One treatment adjunct Bredesen favors is **methylene blue**, which is something I recommend for just about anyone who wants to improve their health and reverse degenerative disease, primarily because it's so effective at reducing reductive stress. It facilitates electron transfer forward in the mitochondria, thereby allowing ATP production to occur, even if the complexes are damaged.

Raising NAD+ is also important for energy production. NAD+ is oxidized, not reduced, so it facilitates the transfer of electrons forward in the electron transport chain. While there are expensive precursors out there, my favorite is plain old niacinamide, which is incredibly inexpensive yet raises NAD+ effectively.

Recent research has also confirmed that **niacinamide** helps slow brain aging. For general health, I recommend taking 50 milligrams of niacinamide three times a day. Niacinamide also works synergistically with methylene blue.

Many dementia patients also have low **glutathione** levels, especially if they've been exposed to mycotoxins or other toxins. I'm not a fan of taking glutathione, because glutathione is reduced, and you need the oxidized form to really make it work.

To make the actual glutathione molecule, you need both cysteine and glycine, so one way to boost your glutathione level would be to take glycine and N-acetylcysteine (**NAC**).

Two other ways to get more glycine into your diet are to eat "nose to tail," not including muscle meat, or taking a collagen supplement or gelatin powder. "Nose to tail" refers to organ meats and connective tissues, which are rich in collagen. Collagen, in turn, makes up about one-third of the protein in your body, so it's incredibly important. About 30% of the collagen and gelatin is glycine, so it's an excellent source.

Precision Medicine Program to Launch

Bredesen is also part of a team launching a Precision Medicine Program at the **Pacific Neuroscience Institute** in Santa Monica, California. The program will work to prevent

and treat chronic conditions at all stages, but will focus on getting people in for prevention and early treatment.

> *"When you get Alzheimer's, you go through four stages,"* Bredesen says. *"You go through a presymptomatic phase, and you go through subjective cognitive impairment (SCI) that lasts on average 10 years. For these areas, prevention and treatment are pretty much 100% effective. We can prevent, and we can reverse virtually every time people are in SCI.*
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> *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. Still, in our trial, we had 84% of those people improve.*
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> *The final stage is dementia. And we still see some people with proof of dementia improve. But the farther you go, the harder it is to get them all the way back. So, we encourage everyone, please come in early.*
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> *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. But we've never seen anyone yet be able to go from zero MoCA, which is end-stage Alzheimer's, to perfect 30 ...*
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> *A guy wrote me a nasty note a couple years ago, saying 'How dare you tell people that if they're too far along, they shouldn't get on this protocol? 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 better.' She could dress herself, she could speak again, she could engage.*
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> *So I don't say there's a limit, but it is much harder below 16. You can get some dramatic subjective improvements. And again, we've seen people go from 15 to 27. So, it does happen, it's just that it's harder the longer you wait, which is why we encourage everyone to come early. If everybody would come in in those first two phases — prevention or SCI — dementia would be a rare problem."*

Sources and References

- [1] Aging September 27, 2014; 6(9): 707-717
- [2] American Journal of Clinical Nutrition March 2023; 117(3): 455-466