Introduction and Interview Overview

Welcome to the Fasting and Longevity Summit. I'm your host, Doctor David Jokers, and today I'm excited to interview Doctor David Perlmutter, who is a board certified neurologist.

He's a six time New York Times bestselling author of. Some of his famous books include Grain Brain, Brain Maker, and Brainwash, and his latest New York Times bestselling book is called Drop Acid, and it focuses on the pivotal role of uric acid in metabolic diseases, and it was published in February of 2022.

Doctor Perlmutter serves on the board of directors, and he's a fellow of the American College of Nutrition. You can find him at Doctor Perlmutter, Dot com.

And today we're going to talk about how to prevent Alzheimer's and extend the vitality of your brain. Obviously, if you're interested in longevity, you need to know how to take care of your brain.

Alzheimer's, dementia, cognitive decline is on the rise. And so many people, as they get into their 70s and 80s, and now even more so in their 60s, they're developing cognitive decline.

They're developing dementia, Alzheimer's disease, disease rates are going up significantly. We're going to talk about why that is the root cause, factors behind why people are having higher rates of cognitive decline, neurodegeneration.

And we're going to talk about some of the key lab markers. We mentioned uric acid. We're going to talk about 3 to 5 other key labs that you want to be aware of.

As you are trying to monitor how healthy your brain and your body is as you are aging and and your risk of developing cognitive decline. We're going to talk about evidence based lifestyle strategies for a healthy brain, and the best foods and nutrients to support a healthy brain.

So you guys are going to love this interview. Please share it with anybody that you know and that you care about. And without further ado, let's go into the interview.

Well, Doctor Perlmutter, always great to, speak with you and, just really excited about, this topic, Alzheimer's disease. Obviously, you know, it's through the roof cognitive decline.

There's so many people dealing with it. I know 6 million in the United States. And that's supposed to go up to to like 15 million by the year 2050. So there's an extraordinary rise.

Why is that? What are we doing? That's that's ultimately causing such an increase in cognitive decline? I would say that there are many factors, and not the least of which is the fact that I think we have our eye kind of off the ball, at least in terms of generally how it's being pursued.

Why Alzheimer's Rates Are Rising

You know, you and I are recording this, our time together today, a couple of weeks before Alzheimer's Awareness Month here in America. And, we're all aware of Alzheimer's, that's for sure.

You know, how could you not be? And I and I think that it's through. You're kind of outreach that you're doing now that we can then really interface with this disease as we should and focus on prevention because we don't have any meaningful treatment right now in terms of any drug that will turn this around or no way to cure it.

And I will say that, you know, there's been a lot of excitement this past year, 2023, with the idea that, there's a sudden breakthrough, this, the can be drug, you know, wonderful breakthrough in Alzheimer's treatment.

And the reality is, when you look at the publication in the New England Journal of Medicine, it doesn't really do that much. People at the 18 month mark, they have looked at about 890 people who got the drug, 898 who did not receive a group.

And when you look at the 18 month mark, there's very, very little difference in multiple markers of cognitive function. Number one. And really interestingly, in the last few months, both groups fall off a cliff and are really, aggressively demented at that point.

And, you know, we always practice medicine. The notion of, above all, do no harm. And that's one thing I think people really need to consider as it relates to this new breakthrough drug.

And that is that the risk of damaging side effects to the brain was fairly dramatic in the treatment group. About 14% develop these multiple areas of small hemorrhage and, swelling in the brain.

Whereas the placebo group, it was less than no was around 1%. So it's a drug that doesn't really do that much. And the downside is significant. Let's be clear.

If there's a drug that's going to help in Alzheimer's patient, I'm all in and count me in to at least look at it in terms of does it work and is it safe.

But we're not there yet. So that said, I really think that when we take a step back and recognize that fundamentally this is not a disease caused by the protein data, amyloid, that's the big news that everybody is talking about.

Let's get rid of the beta amyloid in the brain. And lo and behold, Alzheimer's will go away. Isn't happening. We've got to understand that upstream of the beta amyloid and others before that's an issue, if it's even an issue, are the metabolic changes of the brain.

The fact that the brain isn't able to use fuel appropriately, like glucose? And this is when the brain cells start to suffer and ultimately perish because they're not able to utilize, fuel appropriately.

So I really think that that needs to be our focus. There was an interesting, editorial in the journal of the American Medical Association, recently calling, upon us to first really recognize that this amyloid hypothesis needs to be reexamined, a and B, that fundamentally, we should be focusing on what is called the bio energetic nature of Alzheimer's, that it's metabolism, it's the function of mitochondria, it's preprogramed cell death.

And these are factors that we can target early on in terms of lifestyle, to keep people healthy in the first place. Yeah, it makes a lot of sense. So beta amyloid we see that in the brain with people with Alzheimer's disease.

But it's not actually a root cause factor. It's showing up as a result of these metabolic dysfunction that's taking place. And the increase nutrition.

It's neither necessary nor sufficient to cause Alzheimer's. There are plenty of patients who are whose brains are loaded with beta amyloid on specific types of Pet scans, who are cognitively just fine, thank you very much.

And there are plenty of patients who are clearly suffering from Alzheimer's, aggressive Alzheimer's, and don't really have an abnormal amount of this beta amyloid accumulation.

So, you know, this happened before. It happened in the in the early 1980s when, it was discovered that the brains of, of Alzheimer's patients were low in a particular neurotransmitter called a single column.

So drug companies, really scurried to create drugs that would increase the acetylcholine in the brain. And they targeted an enzyme that would break down these little coli.

And I thought, if we can keep this enzyme from working, then they would be more acetylcholine. And lo and behold, we would fix Alzheimer's. And that became the mainstay treatment, a drug called donepezil, the mainstay treatment for Alzheimer's.

Based on this cholinergic hypothesis. And to this day, it's still the go to drug, even though research has found that use of this drug, donepezil, actually leads to more rapid cognitive decline.

It's just take, you know, and maybe I'm sounding cynical, I am, I, I know I am. It's frustrating for me as a neurologist, as a person whose father perished from this disease.

And, you know, when you look at it from those perspectives, I think I'm, it's fair that I get to I get to chime in and have an opinion. My opinion is okay whether the drugs are working or not.

Let's prevent it on the front end anyway. That's the right thing to do. From a compassion perspective, from an efficacy perspective, and from a financial perspective as well.

Amyloid, Drug Limits, and Brain Metabolism

Yeah, absolutely. And you know, so basically the the current medical system, I mean they're using paradigms, they're a little bit outdated. And so they're they're linking correlation with causation.

And that was a problem with the acetylcholine set. See the choline drugs as well as the beta amyloid medications. And so there's a correlation. But not it's not actually the cause of Alzheimer's.

Now you mentioned meta metabolic disturbance as a root cause. And so let's go through some of the main root cause factors. And kind of really the ones that we can reduce with lifestyle the most.

Well, I think that, you know, let's begin by taking this step back and looking at the big picture. And that is the brain needs fuel like any other part of the body, but it needs more.

The brain only weighs about 5% of total body weight in general, and uses at rest about 25% of our total energy consumption. So it's a very energy hungry computer up there that's taking, a lot of fuel to keep it working.

And it's not just the amount of fuel, but it's the delivery and utilization of that glucose fuel. Now, we can have a discussion later on about the fact that the brain is a bit flex fuel in terms of what it can run on, but by and large it's glucose and and as such, it is somewhat dependent on the ways that cells can utilize glucose, for their metabolism.

So they can do their housekeeping and work and, and connect to other cells and allow neurotransmission and all the things that brain cells do. And in that regard, the hormone insulin is important.

How, insulin affects the brain is many facets, not the least of which is allowing cells to utilize fuel. But I think it's valuable to consider that insulin also is a trophic hormone.

It allows brain cells to be healthy. Basically, it actually allows facilitates brain cells connecting to each other, a process called synaptic agenesis.

So this is one of the trophic approaches or ideas that we think about when we talk about insulin. Yes, insulin is important for glucose utilization. And insulin resistance is correlated with increased risk of brain function decline.

Becoming a full on type two diabetic may be associated with as much as a four fold increased risk for developing Alzheimer's disease, a disease that I mentioned is a disease for which we have no meaningful pharmaceutical treatment.

So that said, we need to keep from becoming type two diabetic, and before that, we need to keep from becoming insulin resistant. We want insulin to do its job, and that means that our lifestyle should be one in which we do

everything we can to keep insulin doing its job.

And insulin is a lazy hormone, if you will. And the more we call upon it, the less likely it is going to be there to work for us. So we don't want to keep stimulating insulin all the time, because after a while, insulin doesn't work as well as it should.

We call that insulin resistance. And so the way to keep from picking on insulin so much is to keep our blood sugars under control. And that means getting to the root of your question, lifestyle choices that keep our blood sugar where they need it to, where it needs to be, and that is eating foods primarily that are not, manufactured, that aren't, ultra processed in terms of the carbohydrates, etc., which would raise blood sugar and challenge insulin.

It means eating foods that are lower in refined carbs and sugars as well, but also eating foods that tend to balance our blood sugars, like good fat. Why don't I just say eat more fat? Who knew?

But good fat? Let's talk about the, you know, the non processed, non modified fats as well and also keeping our gut bacteria healthy. It turns out that the billions and billions of bacteria living within the gut play a central role in regulating body.

Yes. Brain as well. Metabolism. But what's going on in your brain in terms of its metabolic signature right now is, to a significant degree, determined by what your gut bacteria are doing.

Can you imagine what a concept? Therefore, we've got to do what we can to keep our gut bacteria healthy, feed them lots of dietary fiber, not threaten them with various medications like non-steroidal anti-inflammatory drugs and acid blocking drugs and chlorinated water and and issues like that.

So everything that we can do from a lifestyle perspective to keep our blood sugars where they need to be at all times, I think it's going to go a long, long way to keeping the brain metabolism where it needs to be and significantly reducing, risk of Alzheimer's disease by as much as 50 to 70%.

Think about that. A dramatic I mean, if we could if we could say 10%, that's a job well done. I mean, if we could take that 6.5 million Americans already carrying a diagnosis, or let's say, the 55 million people in the world who've been diagnosed, or even then, 10 million new patients every year and drop that number by five, ten, 15%, 20, 50%.

Oh, my gosh, that's a good day's work. I mean, that's the right thing to do. And it's why we're having our discussion today. Yeah, that is really what we need to focus on.

Insulin Resistance and Lifestyle Root Causes

And so somebody out there listening and they want to look at some labs that will help them understand their risk of cognitive decline of insulin resistance.

A lot of the things that you've been talking about here, what would be like 3 to 5 key labs that they should really keep an eye on? Well, you know, let's even take a step back and, recognize that before you even have your labs drawn, one indicator of risk is a very, very sophisticated device called a tape measure.

Put that tape measure around your belly and then put it around your, your waist, and you develop what's called a waist to hip ratio. Higher levels of belly fat in comparison to your waist size, where you don't accumulate as much fat, are strongly correlated with, Alzheimer's risk.

So, yeah, we can talk about labs, but that's simple enough. And I think people may not even need the tape measure. They just need to need to look in the mirror.

With all due respect and recognize that's a risk. Now, that is a manifestation of lifestyle choices, primarily dietary secondarily, exercise and quality quantity of sleep, all impact and waist ratio quite dramatically less so is the metric that still remains popular called body mass index, which I think should really be abandoned because it's pretty

meaningless.

I mean, it wasn't originally developed to have any, relationship or conclusions drawn as it relates to health. Let's look at things like, waist hip ratio now as it gets to laboratory studies.

I think, you know, pretty much the status quo getting back to blood sugar and insulin and all of that is that people go to their doctor annually, have an annual, panel of blood test done.

And included in that is a fasting blood sugar, which I'm not going to say is pretty meaningless. I mean, you if your blood sugar fasting is elevated, you've got a problem.

But, you know, like, now if you're cognitively impaired, you've got a big problem knowing that your blood sugar or fasting is elevated. You're it. Like I say, it's already too late, but you're already in trouble.

So we would like to be anticipatory in terms of where a person is on, in relation to their metabolism, in relation to their sugar balance and insulin functionality.

So to that end, we can predict where you're going to be in a year, three, five years from now based upon some lab studies that we're able to do today.

And what are they? Well, first of all, fasting blood sugar and an A1 C are good. But coupled to that we'd like to know your fasting insulin level. Why?

Because if your, blood sugar looks pretty good, but your insulin levels now starting to climb, it means that your pancreas is working overtime to try to keep that blood sugar in the normal range.

Yeah, blood sugar still looks good. Your blood sugar is 100. You're thinking I'm good to go, but if your insulin is starting to spike at 1214, whatever, it means that your pancreas is working overtime to give you that result.

And it means it's not going to last again, it means two years from now when you come back for blood work or whenever it may be, that finally you're going to develop this insulin resistance and your blood sugar is now going to be elevated, and you're going to say, whoa, we should have known about that.

So you can know to a significant degree by looking at your fasting insulin. Also, people can easily have what's called a five hour glucose tolerance test.

So rather than just know what your fasting blood sugar is, you can be challenged to drink 100g of glucose, which is basically the dextrose. And you then follow your blood sugars through the five hour period and see how you respond to a carbohydrate challenge, and not just how your blood sugar responds should be normal, but it could be elevated.

But how your insulin looks as well during that five hour period of time. So this is a far better way of understanding the dynamics of your glucose metabolism.

With a simple test that any doctor can order. Now, what do I do for myself? I wear what's called a continuous glucose monitor or CGM. It's become, you know, the acronym is pretty popular there.

So I know at any given moment what my blood sugar is. And, and, like, where it is, does it ever get to a place that I'm not completely happy? You bet it does.

Then I ask myself the simple question. What did I do? Well, where did I mess up? I might easily know where I messed up and say, well, it's because of what I had for dinner tonight. I knew it would be bad. It's okay.

Because in general, my blood sugar is great or it could be something going on. My blood sugar that I wasn't aware of, a food that triggered my blood sugar to spike, that I wasn't expecting for in my case, like, no cashews.

Cashews breaks my blood sugars. Very surprising eating eggs with lots of olive oil in my case, for whatever reason, looks like it drops my blood sugar.

So that's great. It's an intervention. I can I can use quercetin. I think it's dropping in my blood sugar as well. The point is that I know where I am and I know what's controlling my blood sugar.

I'm clearly, impressed that my blood sugar goes up when I exercise short term. Then if I don't have a good night's sleep, which is rare for me, I happen to sleep pretty well that my blood sugar will be elevated the very next day.

And it's just a call for me in my outreach, like you and I are having right now, for people to think about the quality quantity of their sleep, if their blood sugar is coming up, or even before the blood sugar comes up.

Sleep, we'll talk about in a minute. So these are some of the important tests, I think looking at markers of inflammation, like C-reactive protein clearly correlated with, Alzheimer's risk.

Great. But the question is, so what do you do about that? Oftentimes, an elevated C-reactive protein or CRP, highly sensitive, relates back to elevation of blood sugar.

Who knew why? When blood sugar is elevated, it binds to various proteins in our bodies called glycation, a process called glycation. And our immune system then sees these proteins perhaps as being foreign.

They don't work as well as they should, and that turns on inflammation. You might measure that in the C-reactive protein. Now, this may sound complicated, but the a1 c test is a marker of glycation in protein in this case hemoglobin.

So that makes it more, understandable and familiar to viewers. So it's a very common test. The A1 c is valuable. It gives you a longer term sense as to what your blood sugar is doing.

So I think these are the keys. There are a lot of others, along with uric acid being fundamentally important for metabolism. And we'll talk about that at that link that kind of left off the list for now, because I know we're going to get back to uric acid.

I think it's really very important. There are many, many other tests, not the least of which is knowing genetically what you're at risk for elevation of things like homocysteine, a really important marker of risk for cardiovascular and, Alzheimer's diseases as well.

So homocysteine certainly want to include that on the list along with, you know, more esoteric things that really depend on an individual's genetic predisposition.

Yeah. It's a great list that you gave us. And that continuous glucose monitor really gives personalized information. So you can see there are certain foods that you might think spike your blood sugar and they may not.

And there are other foods that you might not think and they would like. I know with my wife, honey, seem to be fine. And then she took maple sirup and that spiked her blood sugar.

Her blood sugar went way up, and she did the same amount of honey. And it didn't. And I know for me, I have a certain caffeine amount when I when I go beyond that threshold, my blood sugar goes way up.

And so you kind of you're able to to personalize it and get that instantaneous biofeedback to really create a program that works best for you. So I think that's a great suggestion.

The waist to hip ratio. Understanding that really just being able to look down and see your toes, that's a sign that you're not going to have as much visceral fat, that inflammatory fat around your organs.

So those are great suggestions. Let's jump back to uric acid.

Key Labs for Brain and Metabolic Risk

I know you wrote a whole book about this. And most medical practitioners, when they think about uric acid, they think about gout. And this condition of gout.

Right. But in your book, you laid out the research and how it's related. Elevated uric acid is related to all these different types of metabolic diseases.

And in particular, a lot of these neuro degenerative conditions. It's really, I think a fascinating story because, you know, we all learned about uric acid in one hour, that it's a bad thing.

And if it's elevated, you get gout. And here's the drug that was basically the messaging. That was pretty much my understanding of uric acid, though, over the years we started to see research, you know, and decades, that related uric acid levels to risk for certain, issues and even reduced risk for certain issues like Parkinson's.

What we can maybe unpack graphically if we can. But more recently, there's been a flurry of research looking at uric acid from a totally different perspective, through a different lens, through the lens of metabolism, and even historically through the lens of our survival.

And it's a it's really an elegant, development of a story, because it turns out that our primate ancestors were threatened with starvation around 8 million years ago when the world suddenly cooled.

And those of our primate ancestors that had higher levels of uric acid tended to survive. So it was environmental pressure to seek out those individuals or to select them for survival when they had a higher uric acid level.

Because higher uric acid allowed them to make more body fat, a caloric storage depot as a hedge against starvation. In addition, higher uric acid raised their blood sugar, which over the long run proved to be a good thing to power their brains.

We talked about that earlier so they could avoid two things starvation and predation, meaning they wouldn't, run out of food and they wouldn't become food.

Two things that your ancestors and primate ancestors would have really focused on. It turns out that uric acid, then, when it was elevated, protected them to some degree.

And how it happened genetically was that these primates lost the genes. That coded for an enzyme called year case, an enzyme that would otherwise have broken down and lower that uric acid.

Now, you and I and everybody else on the planet have lost the case enzyme. So we don't have this enzyme for breaking down uric acid as a survival mechanism, as a hedge against starvation.

But this becomes in a powerful what we call evolutionary environmental mismatch. From an evolutionary perspective, it's great to have this, genetic change that allows us to survive if we don't have food, and less so, as if we don't have water.

But these days we are triggering this uric acid accumulation left, right and center. And as you learn and I learned, to lower uric acid, we have to put people on a low purine diet.

Right. Remember those? Yeah. And that would mean lower levels of, you know, lots of meat and high peri foods like yeast and shellfish and small fish, etc.

and that's still and messaging on many of the large, well-renowned clinics websites that you go on a low hearing diet. That's not it's not the elephant in the room, the elephant in the room.

What really raises uric acid is a sugar called fructose fruit sugar, because it was the fructose sugar that even

allowed the survival of our ancestors.

That's the sugar that becomes available when fruit ripens. And, in the end of the summer and the early fall, that is instruction for your body that winter is coming, make and store fat and ratchet down your energy expenditure and turn on the process of creating more glucose in your body to power your brain and raising your blood pressure as a hedge against dehydration.

That's what's triggered by fructose. We are consuming fructose like never before. The amount of fructose we in Western cultures consume. Now is is mind boggling.

No doubt in part as a consequence of the development of high fructose corn sirup. A very, very sweet and very inexpensive sweetener that has found its way into probably 60 to 70% of packaged foods in one form or another, here in the United States.

So we are bombarding this system, triggering this system to make us believe that winter is coming and we've got to make fat store fat reduce our utilization of fat for energy, ratchet down mitochondrial function, raise our blood sugar, raise our blood pressure as a consequence of the signaling that we're doing to our bodies.

By consuming high levels of fructose, which is metabolized into uric acid. What is story about uric acid? So, you know, getting back to our original conversation, that been a high level of uric acid would threaten metabolism.

And Alzheimer's is primarily a metabolic issue. It's a problem with respect to glucose utilization, insulin functionality in the brain. Now with having a high uric acid be a threat to the brain?

You bet it is. In the Annals of rheumatic Diseases, in 2018 was published a powerful study of 1600 individuals that were followed for 12 years. A large group of people followed for a long time, and what they did in the beginning of the study is they measured their brain function and they checked their uric acid level.

Pretty straightforward study. About every two years thereafter, they again checked their brain function. And indeed, many of these people had MRI of the brain.

So not an inexpensive study after, the the study was completed. So here we are 12 years later.

Uric Acid, Fructose, and Dementia Risk

I mean, that's a commitment to do a study for 12 years, it was revealed that those individuals who had the highest uric acid at the beginning of the study had an 80% increased risk of developing dementia.

They had a 55% increased risk of developing, specifically Alzheimer's disease. They had a 165% increased risk of developing what's called vascular or mixed dementia.

Makes sense? Uric acid threatens blood vessels. Blood vessels need to work in the brain when we see defect. Defects in the blood vessel functionality that can lead to Alzheimer's disease.

So this shows a strong relationship then between having a uric acid level and then 16 years later, being at a dramatic increased risk for having your brain fail.

So again, getting back to your question, that's why uric acid is on the list. Yeah, it's a key biomarker. And people can go in. They can ask their doctor if you've never had that done before on your routine blood work, you can ask, that's pretty inexpensive add on.

And for most people their insurance will cover it as well. And what would be the ideal range you'd like to see it in? Well let me, I'll get there in a second.

But I think what you said is very true. But I would add to that that, most people, oddly enough, in their annual blood

work, have a uric acid checked.

And again, it's checked in the context of gout, you know, are you at risk for gout? Right. And the the so-called level below which you're at much less risk of.

Yeah. Is seven, point zero, milligrams per deciliter. Now, to answer your question, the cardiovascular metabolic risks begin at around 5.5mg per deciliter.

So we want to keep uric acid levels below that number 5.5. Those are the the units that are used here in America. Yeah. So easy add on uric acid. We want to make sure we're getting that under 5.5.

And think about your fructose content. If it is elevated and look to see where you're getting so much fructose corn sirup like you mentioned, hyper dose corn sirup.

A lot of these processed foods would be the main culprit. You know, fruit to a lesser degree. But, you know, clearly it's for some individuals, metabolically, they could probably overeat on fruit as well.

Is that correct? You can. That's right. But it's kind of like is it tough to do. You're going to get about five grams of sugar in an apple and when you consume an apple, you're not just consuming the sugar, but you're consuming fiber.

Dietary fiber then obviously gives the microbiome, but it slows the absorption of that, specifically fructose in the small intestine, to the extent that it's not going to really allow enough of a bolus or increased amount of fructose, that much is going to get to the liver where this transformation to uric acid is taking place.

So have an apple a day that will keep the doctor. What are some oranges but not orange juice. So orange juice has, you know, 12 ounce glass of orange juice has 36g of sugar, just like your favorite cola drink or any, you know, the soft drinks.

So what's the the beauty of it? What's the good of it? Well, people say, oh, it's got a lot of vitamin C and all that stuff. Well, it really doesn't have much vitamin C at all and it doesn't have much fiber in it.

And so no, if you're trying to relate this to the experiences of our ancestors, they wouldn't find bottles of orange juice hanging from the trees and therefore, you know, imbibe all this fructose and challenge your body and higher levels of uric acid.

So have fruit, you know, no question about it. Fruit's a good thing. Blueberries always been on my list. And, there are a lot of important reasons to be consuming fruit, but, you know, do you go overboard?

Yes, you could, but I think that it's valuable to consider if your body can be forced into actually producing fructose and therefore elevating its own uric acid.

That doesn't sound like fun at all. I mean, here you are totally avoiding fructose. Next thing you know, Doctor Perlmutter is onto, you know, on a presentation saying your body is going to make fructose.

Oh my gosh. And I think that it does. So under a certain set of circumstances. There is a pathway called the polyols pathway in which your body will convert glucose blood glucose into fructose.

And that doesn't sound good. And it's not. And the body will do that when it thinks it's dehydrated. So when the body thinks it's dehydrated, it certain enzymes are activated altos reductase in this case.

And what that does is it converts, glucose into fructose. And why might your body think it's dehydrated? Well, the main metric that the body's physiology uses to determine your level of hydration is the sodium content.

And you can be sure that when you park yourself in front of the Sunday afternoon football game and start eating

that bag of pretzels or chips that are highly salted, your sodium goes up, your body thinks it's dehydrated, and the next thing you know, you're converting glucose and fructose.

Why would your body want to do that? Interesting, right? Why would you want your body fixes dehydrated? Why in the world do you want to create fructose?

Well, like a triage response, right. To kind of yeah. Well what is fructose become? It becomes uric acid. And that triggers the body to make fat fat. Right.

And why in the world if you were facing constantly facing dehydration of all things, why would you want to make body fat? Think about that. What's the point? I can't find water month after month.

Why is my body triggered to make more body fat? Because when it does so and you burn that body fat, you create two things carbon dioxide and water. You're actually, providing yourself what's called metabolic water.

You're creating water in your body. I mean, here's how you can understand that. If here's an animal that can walk across the desert, the Sahara desert, for weeks at a time without drinking water because it has a huge hump on its back, obviously, I'm referring to a camel.

And if you put a biopsy needle in that hump, does the water come gushing out? No. It's fat. That's what's in the camel's hump because the camel is able to use that body fat over weeks time to create the water that it needs, the metabolic water such that it doesn't become dehydrated.

Whales have eyeball receptors. Yeah. And they don't they don't drink from underwater springs or anything. They're making metabolic water from their body fat.

So that is let's just understand this powerful correlation that we see in children and adults between eating a high salt diet and obesity. Now it makes sense.

Now we and I love this because we you know, we knew that was happening, but we really didn't understand why. Now we've connected some important data. We have to spend less time trying to figure that one out, because now it makes sense.

Yeah, it's really interesting. It's a survival response. And my hypothesis would be that it's a high salt diet in also going on with a higher blood sugar.

Basically a higher blood sugar, more insulin resistance taking place. So high salt and highly fed state, I would imagine. More so than a high salt fasted or kind of, lower carbohydrate style diet.

And I would agree with you because I think that again, we're triggering, ultimately fat metabolism. Yeah. So I think that you are correct. But I think it gets to the point of you know, overdoing salt and its relationship to, to blood pressure.

And there are a lot of mechanisms that have been invoked, that relate salt consumption to high level sodium to raising blood pressure. But when you trace this, as we've just discussed, through this pathway, that creates fructose from glucose to uric acid, how does that then relate to blood pressure, which it does because it's a survival mechanism. We can't find water.

We're going to ultimately not produce our organs. Our kidneys are going to fail, our brains and fail, etc.. So we get these mechanisms going that raise the blood pressure so we can survive.

And this is a very powerful relationship between elevation of the uric acid and compromise of the body's ability to use what's called nitric oxide or no.

So this relatively new science, the Nobel Prize, of course, was awarded based upon the discovery that nitric oxide

regulated vascular tone. And, beyond that, you know, that that science, that chemistry has really been teased apart and analyzed.

We recognize that aside from that, nitric oxide really playing a central role in regulating how insulin gets out of the blood vessel into the cell and actually how, both of those, pathways out of the blood vessel and into the cell are regulated by nitric oxide availability and functionality that is compromised by higher levels of uric acid as a survival mechanism.

Yet again. So when we have a high uric acid level, which, as I indicated earlier, is associated with a dramatic increase in brain decline in 55% increased risk of Alzheimer's, exactly 165%.

Increased risk of vascular blood supply, dementia. Now that we understand this nitric oxide connection, we say to ourselves, well, now I can get my arms around the literature that shows the profound, damaging effects of a high fructose diet on the brain, not just in terms of Alzheimer's risk, but in terms of cognitive function.

Right now and in terms of brain degeneration. You get it. You understand these relations because now we have that lens, the nitric oxide lens from uric acid being elevated.

That's making this stuff understandable. And, you know, I find that to be very exciting because once these pieces fall into place, when you're discussing with people the notion of lowering your dietary fructose in, they may or may not want to know here's why.

But if they do, you can explain it and get excited about it. But I think the take home message for viewers right now is you've got to seek out the hidden sources of fructose in your diet.

Is it the sauce? Is it the condiments? Is it the prepackaged goods that have all kinds of names added, that are trying to take you off off the scent here?

Funny names for sweeteners that you might not, recognize. And, you know, these manufacturers are very crafty in sneaking that sugar in there and so you don't recognize it.

But again, it's the the validity and the value of shopping the periphery of the grocery store and getting things that aren't packaged, getting fruits and vegetables that are packaged meats and fish, etc., if that.

If you choose to eat meat, fish, poultry, etc.. Yeah, it's really interesting.

Brain-Supportive Foods and Supplements

But the nitric oxide relationship and so like you mentioned, we want to avoid the fruit juices, concentrated fruit juice, but eat the whole fruit. And in the whole fruit you're going to have more polyphenols, more antioxidants like an apples.

You've got quercetin. You mentioned that earlier and that's one of your favorites. You got raspberries trial and you know some of your berries like blueberries and anthocyanins and things like that.

What are some of the key nutrients that you recommend for people and key foods as well? Just foods. And then also go into maybe some supplemental nutrients as well, for helping prevent against cognitive decline.

Sure. And in a word, I'd say complexity. So let's tease that apart. Let's make it less complex. But complexity is what you find in food complexity of an apple with breaking it down to, as you mentioned, the flavonoids, the fiber, the various vitamins that it contains.

Yes, the carbohydrates as well. That's what we're looking for. We don't want to find foods that have been processed to to simplicity, you know, simple carbohydrates, for example, highly processed or ultra processed foods are a huge threat to our metabolism, and they are a huge threat to the brain.

They are powerful. They're powerfully related to dementia risk. But yet in America, about 55% of calories are derived from this very dangerous group of foods called ultra processed.

And, you know, no one's screaming about that. And we should, because this sets the stage not just for brain degeneration, but for all manner of chronic degenerative condition, be it coronary artery disease, cardiovascular disease, cancer, diabetes, obesity, and certainly cognitive decline as well, which, you know, as a group, the chronic degenerate conditions are ranked as the number one cause of death on our planet by the World Health Organization, with upstream of that being these ultra processed foods.

That's really important. I have the opportunity to speak at the, world Bank and International Monetary Fund on this exact topic. And, you know, I tried to emphasize that it's not just bad medicine, but it's bad economics as well.

I mean, you know, we're spending probably $350 billion a year right now in America to care for Alzheimer's patients. And by by 2050, that number isn't to be anticipated to be $1 trillion a year.

And that doesn't take into account the emotional cost. You know, we you know, we need to think about that as well. Been there, done that. And I can tell you that it's it's an extremely important as well.

So as relates to your question, as relates to food, I like, complexity. I like the fact that there's a lot of things in, you know, in colorful food complexity of the appearance of your plate, many, many different colors.

Now, as we get to the three macronutrients of protein, carbohydrate and fat, I think it's fair to say we need, a good slug of protein, the body needed to maintain its muscle mass.

We need to keep muscle mass because muscles are an endocrine gland secreting chemicals that are good for the brain. So good levels of protein. You know, I choose to eat fish.

But you can get protein from plants, that's for sure. Very important. There are things in meat that I think are good for the body. Things like vitamin B12.

So those of your viewers who are not eating meat should consider using, for example, a B12 supplement. Animal products, have nice levels of good fat. And it was, you know, only recently that the idea of good fat was sort of an oxymoron.

Yes. We need we desperately need fat in your brain. Not just your brain, but everyone's brain is about 70% fat. And it doesn't come from the air. It comes from the foods that we eat.

Fat is physiologically very important for building cell membranes, like the membranes of brain cells. But also controlling inflammation is a powerful mechanism related to brain degeneration.

We need lots of good omega threes. Hence my desire to eat a lot of, salmon. But you can take an omega three supplement. I do, I take a visual supplement, but there are vegetarian options available to give people plenty of, DHEA and secondarily, DPA and EPA as well.

So, again, I cannot overemphasize the value of vegetables and to a lesser extent, fruit as it relates to taking care of your gut bugs. Those gut bacteria are regulating your brain's ability to use glucose.

Think about that. All of our discussion thus far on the, the pivotal role of brain metabolism in terms of keeping your brain functional, and functioning, that a huge input is the health and functionality of your gut bacteria.

That's why nurturing them with fiber rich food is so important. And eating fermented foods that actually contain the bacteria, one of my favorites is kimchi, but it could be sauerkraut.

It could be other forms of fermented vegetables. Good sources of bacteria dates back to our time as a hunter gatherer. You know, if our hunter gatherers were, we're starving.

They're not going to turn their back on the, on some fruit or vegetable on the ground that happens to be rotting. What is rotting? Rotting is fermenting.

And we've all tasted a rotting, accidentally tasted a rotting food. And it to some degree, you know, you can you can taste that. It tastes a little bit sweet and may even have some alcohol in it, because that's what goes on when food ferments.

So, fermented foods important. And again, back to dietary fiber. So that's a protein. That's a carbohydrate and that's the fat. Those are the key macronutrients.

I wish fiber was considered a class of macronutrient, but it is by definition a carbohydrate. But it's so important to emphasize that, you know, in America where people are consuming 20g of fiber a day, and that's probably about a quarter to a fifth of what we really need to be consuming.

Yeah, for sure. So definitely, getting the vegetables, getting the meat, like you talked about the protein. Well, you don't necessarily need meat, but getting good quality protein, healthy fats and most people in our society, we've lost that flavor for sour.

Right. But all of our ancestors were consuming fermented foods and getting that kind of that sour flavor. And as you start to eat like this, you actually start to crave it.

I know for myself, I love kimchi pickles. My kids do, you know, most people, their kids are just craving sugar all the time. But if you start giving them fermented foods, my kids, they ask for pickles, they ask for for sauerkraut and things like that.

So, we kind of reawaken our natural desire for those types of foods as you start to incorporate them. So great list. What would be, let's say, 3 or 4 of your top supplements.

You mentioned omega threes, B12 outside of those, what would you what else would you say for people to look for, particularly if they're at risk for cognitive decline?

They're looking to, to, to really take up their health. They're following some of these lifestyle principles. What should they look for? Let me first address what you just said, which is, for those individuals who are at risk for decline, that's everybody.

True. It really is. Everybody. And that's a. Smart way to live, right? Hey, I mean, because it's the same approach. Yeah. The risk of cardiovascular disease, cancer, diabetes, obesity, it's all the same.

There's not a unique heart smart diet that's not good for your brain or whatever. So, you know, I think what you mentioned very important that the omega threes are important.

I think vitamin D is important. Quercetin very important, very valuable. I take 500mg a day. I think a good probiotic is reasonable as well. And I think beyond that. B-complex.

Also very important in my case, and probably in the case of probably 20 to 30% of people that should be methylated b-complex because if you look at your genetics, which should be maybe considered part of your lab studies, getting back to that part of our discussion, about 20 to 30% of people are at risk for elevation of their homocysteine.

We talked about that as a lab just earlier. By virtue of some differences or variations. That's a better way of saying it, of their genome. And I happen to be one of those individuals who, because of the way my body responds to B vitamins, requires a different type of B vitamin called methylated B vitamins.

So I take a B complex that has methyl folate and methylated B12 because it helps them because of my genetics. And again, probably, you know, to a third of your viewers, helps reduce risk of homocysteine, a regular B complex

because of that gene quirk that I harbor, would not be as effective.

So be good to know, know your, you know, that genome and the part you want to pay attention to is the part that relates to elevation of homocysteine. And maybe people have heard of something called MT MFR.

Daily Routine and Final Advice

It's pretty popular on the internet MT for, not to be too technical about it, but this methylene tetra hydrophobic reductase enzyme variations can put a person at risk for higher levels of brain threatening homocysteine.

I know it's a lot to talk about, but I think a b-complex is good. I like vitamin D, I take an omega three every day. I take quercetin, and a probiotic and magnesium three and eight.

I'm just thinking about a box and, you know, that's the core. Those are the core players. I use other things that aren't necessarily considered vitamins per se, but I supplement with, a prebiotic fiber that's made from acacia and baobab.

Put that in a glass and consume that along with. Well, now I'm adding more collagen. But, you know, these are things like, I don't even consider that a vitamin or supplement.

I do take a very good multivitamin as well. Yeah, yeah. That's great. I was going to mention magnesium. If you didn't, I know you threw that in there.

That's so key as well. Now last question. Take us through a day in the life of what you're doing on a regular basis, kind of your daily pattern, what you're doing on a daily basis.

I know my listeners would love to know what you're doing as you go through your day. In the life. Great song. The Beatles, I wait from the moment I open my eyes, I turn to my left and I generally look at my wife who's sleeping, and I truthfully, I like I just love the fact that she's still peacefully sleeping.

But then I get lonesome and I kind of making some movements and waking her up and, oh, you're up now. And then we talk about what we're going to do, for the day.

And, we get up and we have coffee, and then we do readings, from any number of, resources, generally focused on, gratitude. Some of the readings are kind of cultivated for that particular day of the year, and others are more general.

And there may or may not be at that time meditation and depending on what our schedules are like. And after that, I, I usually gravitate towards exercise in the morning.

For me, it works better if I exercise late in the day. Kind of jazzed me up a little bit too much. And, so I do, depending on what I'm going to do that day.

I mean, I either will, elliptical at home, bike or, run or go to the gym and elliptical at the gym and lift weights at the gym. That's kind of an every other day alternate day, kind of a thing.

I then, you know, usually take care of, odds and ends doing a lot of rebuilding work on our house. Having had a hurricane last year, still not quite done with that.

I've become very handy. I want you to know, and generally, won't eat until 12 1 or 2 p.m.. And at that point, it might be some, fish, protein, or it might even be a salad.

And then, usually by after noon time, I do my podcasting. I get to interface with people like yourself. I go on other people's podcasts, I write, my blogs and work on whatever book I'm working on or whatever research.

And frequently, during the week, on any particular day, I might have 1 or 2 board meetings that are virtual. So I do those as well. I've over the past recent couple of years, joined some really exciting boards that are looking at things like we've talked about that example, nitric oxide, that science is so cool, and I'm so excited to be part of that research, working with another research group at UCSD on ways of interpreting signaling from the vagus nerve, and how that relates to the health and functionality of the organs in the body.

I'm working on a project, of our yellow sugar, and how that can actually be a positive metabolic experience with a company called sugar. So there's a lot of things that, that keep me busy.

I do spend some time, each week interfacing with, other, physicians who may have a challenge with respect to their practices or with respect to a patient that they're dealing with.

And I really enjoy doing that because, you know, it's a contribution that I make and there's no obligation on my part to. So, I like that an awful lot.

Yeah, that's so good. And Doctor Perlmutter is at a point in his life and career where he could be retired. But all of these things give him joy, and they all support his brain as he's learning.

He's developing new neural synapses, helping prevent against cognitive decline. Alzheimer's and dementia. So he could really live as best as he's, getting up there and age.

And so, Doctor Perlmutter, wonderful interview. Any last words of inspiration here for our audience? Yes, I would say that. Please recognize that each and every one of you is the architect of your brain's destiny.

And you know, the notion of offloading that responsibility to others, as in, you know, people developing a drug here or there isn't going to be helpful, at least in the near term.

So we've got to be empowered to make the right decisions. And each and every one of you can do that. Wonderful. Thank. Thanks so much guys. Check them out.

Doctor perlmutter.com. Thanks again Doctor Perlmutter and we'll see you in a future interview. Be blessed everybody.