THE MODEL HEALTH SHOW

EPISODE 612

Nutritional Therapy To Protect Your Brain And Metabolism

With Guest Dr. Dominic D'Agostino

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SHAWN STEVENSON: Welcome to The Model Health Show. This is the fitness and nutrition expert Shawn Stevenson, and I'm so grateful for you tuning into me today. Our brain health affects every single area of our lives. It is really a master controller of so much about us. From our metabolism to our mood. For example, we have a master gland sitting in our amazing brain called the hypothalamus, and it's the kind of the tip of the spear when we're talking about the hypothalamic pituitary adrenal axis. This information superhighway that has so much to do with our emotions, how we feel, the expression of hormones and neurotransmitters, because there's an integration that takes place in our hypothalamus with our nervous system and our endocrine system, and our nervous system has to do with our feeling, our understanding, our sensing of the environment, our sensing pain and pleasure, and all those type of wonderful things.

Then we have our endocrine system that's associated with our hormones, also having a lot to do with how we feel, but now we're talking more in the language of a chemical messenger system with our hormones instructing all of ourselves on what to do, what kind of behaviors should be taking place within our cellular communities, and that association how's everything intermingling, connecting, getting to know each other. So, we want those hormones to be in balance or could be straight chaos. It could be like a really bad game of telephone. I don't know if you remember that game. You were a kid where somebody starts... Maybe it's the line of 10 kids. Somebody starts with, maybe it's, "I really like toys" and then the next kid whispers it to the next kid, and by the end of the line, after it passes from kid to kid to kid, "I like toys" suddenly transforms into "I want to Rolls Royce" and the picture, I am with DJ Khaled, another one, we got the stars on the ceiling and the whole thing, it then turn into something totally different, passing the message from person to person or from cell to cell, from hormone to hormone, we got to make sure that these things are dialed in because it's going to have a deep impact on our cellular information.

And this is the most important part, because even when you think about food, it's not just food, it's information. It's cellular information. It's going to instruct our cells on what to do based on what we're putting into this brilliant system that we all such a great honor and privilege to have this experience as a human being right now, regardless of all the craziness going on in the world, because we have this innate intelligence that we're just teeming with it. And the more that we get in alignment with it, the more that we really start to feel like life is magical, and we live in conditions where we can start to thrive instead of just trying to survive. So, all of this, again, starts with the health of our brain. Our brain is impacting our mood, it's impacting our metabolism, it's impacting everything about us. Now, what if there was a

framework? What if there was a nutritional framework that can support our cognitive function, even with deep metabolic or even physical damage to our brains.

Right now, many people are unaware, but Alzheimer's disease and neuro-degenerative diseases of the brain are at all-time highs. They just keep getting higher and higher and higher. So much so that Alzheimer's right now is inching its way into the top five leading causes of death for our citizens here in the United States. The degradation of our brains. What if there's a diet framework that can supplant that even with degradation to the brain and re-energize the brain, re-energize the brain's cognitive functions, our memory, our ability to have focus and concentration and all these different things that tend to get lost as the brain is degrading. What if there was a diet framework that can help to address our chronic levels of mental health issues that we're experiencing as society today as well. Again, bypassing the normal routes of treating a symptom through a pharmaceutical that's addressing maybe one neurotransmitter when we've got dozens of other neurotransmitters that are playing a role in that mental health state that the person is experiencing?

So, it's like throwing darts in the dark, medication-tipped darts in the dark trying to hit something. What if there's a diet framework that can help to address the myriad of neurotransmitters that we are producing, the mobilization of those neurotransmitters or hormones and the like really putting our body into a state of balance? Well, that's what we're going to be talking about today with the leading expert on this subject matter in this particular diet framework, and I'm really excited because this conversation is a long time coming. It's one of those things that this is an important thing for us to have in our superhero utility belt.

Whether we subscribe or utilize a diet framework or not, we need to know about this for our loved ones, or our friends and family, individuals that are experiencing mental health diseases, that are experiencing conditions like epilepsy, that are experiencing cognitive decline. We need to have this knowledge base right here on hand so that we can utilize it when necessary, and the occasion for that has become more and more apparent today more than ever. So, again, really, really excited about this episode, but when we're talking about cognitive performance, there are tried and true things that increase the health of our brain, and there are tried and true things that decrease the health of our brain. One of these categories that can either make or break the health of your brain, your cognitive performance is a category of sweeteners.

Yes, sweeteners impact the brain more profoundly than just about any other place in our bodies. It's because even though the brain is protected, you have this external protection with the brain being the only organ that's fully encased in hard bone, but we have internal protection in the form of the blood-brain barrier. The blood-brain barrier has a plethora of sugar gates that allows glucose in in droves. Now, we evolved not having access to this kind of

sugar, but the brain does what the brain does, it's going to gobble up that glucose because it's literally multiple galaxies of activity that's going on in our amazing brains, right? Trillions! It's so much going on, it's so miraculous, it's amazing, it's beautiful. And with that said, food is not just food, it's information. And the human brain, even though it's only about 2% of our body's mass, it will gladly consume about 20% to 25% of the caloric energy that we take in. In particular, some of the latest research has found that the brain can consume upwards of 50% of the glucose that's coming in from any given meal, it's just going to shuttle that right to the brain.

So, with that said, the quality of sugar that we're utilizing, our sweetener, can absolutely make or break our brains. Right now, in the United States, the amount of sugar that we are consuming, I'm just going to say it, it's gotten insane in the membrane, alright. Insane in the membrane, insane in the brain, shoutout to Cypress Hill. Alright, it's absolutely crazy. The latest statistics show that the average American consumes about 70 pounds, 70 pounds of added sugar every year, 70 pounds of added sugar. That's sugar added on top of the already existing sugar in, what most people are eating is predominantly ultra-processed foods. 60% of the American diet today is now ultra-processed foods, sugar-laden, toxin-laden, artificial ingredients, the whole nine. Plus, you add that sugar on top of that, it's a recipe for disaster. So, with that said, that amount of sugar exposure is wildly inappropriate. We can ratchet that down, but also if we look at the tried-and-true sweetener that... And what I'm going to share with you is truly remarkable, and a lot of people don't know about this, because there really is nothing else like this on Earth, and this has been on Earth probably longer than us versus the highly refined sugar that we see on store shelves which is a recent invention.

What I'm talking about is raw honey. Unlike other sweeteners, raw honey has been found to actually improve insulin sensitivity. A recent study published in the peer-reviewed journal; Nutrients detailed how raw honey intake can improve fasting blood sugar levels. Sugar shouldn't do that. But it's not just sugar, there's something really special about raw honey. It's found to improve fasting blood sugar levels, improve lipid metabolism, and reduce the risk of heart disease. Again, published in one of our most prestigious nutrition-related journals. Additionally, the scientists noted that the vast antioxidant and anti-inflammatory properties that honey has is one of the stand-out reasons that it's able to help to reduce the risk of heart disease. On top of that, research cited in the journal, Evidence-Based Complementary and Alternative Medicine determined that honey antioxidants have nootropic effects such as memory enhancement.

Plus, a randomized double-blind placebo-controlled study revealed that honey was able to outperform a placebo and significantly reduce cough frequency and severity at night and improve sleep quality. What can't it do? How sweet it is. The key here is raw honey. The key here is you've got to understand what's out there on the market today because most people

are unaware, not just of the benefits of raw honey, but also that a lot of conventional honeys, even if they're organic, that are out there on the store shelves are unfortunately exposed and riddled with other contaminants, not just... Organic means it's not sprayed with pesticides and herbicides, and that's not used in the pollination, in the process where the bees are getting the honey, that whole thing. But there can be other contaminants like heavy metals, like arsenic, like lead, like mercury, E. Coli, bacterial overgrowths, Salmonella, yeasts, molds, all these things that should not be coming along with the incredible benefits you could be getting from raw honey.

Where I get my honey, my Superfood Honey, so it's not just high-quality raw honey, it also includes some of the propolis and pollen. They are utilizing third-party testing for over 70 pesticide residues and other common pervasive contaminants. Again, like DDT, like heavy metals, so we're making sure that we're getting the best honey possible, and you know the difference. It is phenomenal, I love... I absolutely love my Superfood Honey coming from Beekeeper's Naturals. Go to beekeepersnaturals.com/model, you get 25% automatically taken off at check out. Go to B-E-E-K-E-E-P-E-R-S naturals.com/model, getting 25% off, it's outrageous. They have to do that? 25% off? Amazing, amazing, and they're doing stuff right. Head over there, check 'em out beekeepersnaturals.com/model for their Superfood Honey. I absolutely love their propolis for the immune system. It's another thing to definitely check out. Head over there and add this to your superhero utility belt. And on that note, let's get to the Apple Podcast review of the week.

ITUNES REVIEW: Another five-star review titled, "I never missed a show" by No Comprende. "This show should be mandatory listening for everyone in this country, as well as all health practitioners and practicing doctors. Why there is such a disconnect between the medical industry and nutrition is confounding and infuriating, and Shawn is our hope to bridge this gap. I love this show and adore Shawn's innate ability to translate this information with humility, grace, and humor. I will never miss a show. You've got me on-lock Mondays and Wednesdays, Shawn. Thank you."

SHAWN STEVENSON: No, thank you. That's amazing. Every word. I appreciate it so much. And thank you for taking the time to leave that review over on Apple Podcasts. Listen, if you're yet to do so, pop over to Apple Podcast, leave a review for The Model Health Show. Make sure you're subscribed, so you don't miss a thing, because we are just getting warmed up. On that note, let's get to our special guest and topic of the day. Dr. Dominic D'Agostino is a tenured associate professor in the Department of Molecular Pharmacology and physiology at the University of South Florida and a visiting senior research scientist at the Institute for Human and Machine Cognition. He received his Bachelor's in nutritional science and biological sciences and his PhD in neuroscience and physiology at Rutgers University.

His laboratory develops and tests nutritional and metabolic-based strategies for neurological disorders, cancer and for enhancing safety, resilience, and performance of military personnel in extreme environments. Dom, as his friends call him, was a crew member and researcher on NASA's Extreme Environment Mission Operation, and he continues to do research with a variety of high-profile agencies. Let's jump into this amazing conversation. We're about to nerd out. Get ready to really zero in, get focused, because we're going to dissect some domains of science and neurobiology that few people truly understand. It's very, very important, very powerful. Let's hit up this conversation with the amazing Dr. Dominic D'Agostino. Alright, Dom, thank you so much even coming to hang out with us. It's so awesome to see you.

DR. DOMINIC D'AGOSTINO: Great to be here, Shawn. Thank you.

SHAWN STEVENSON: Listen, you know that the health of our brains impacts every area of our lives. And right now, in addition to that, neurodegenerative diseases have been skyrocketing in recent decades, in particular Alzheimer's disease. I was just looking at some of the statistics before the show today, and it's creeping its way into the top five causes of death in the United States, and yet most people have no idea of this kind of hidden epidemic right now. So, first of all, I want to ask you, if you could, just share a little bit about what is creating Alzheimer's disease from what we know with science today, and also what are some of the things that you've been doing and talking about and teaching about that can help to address this epidemic?

DR. DOMINIC D'AGOSTINO: Sure. Yeah, thanks for asking that. I've never really started off talking about Alzheimer's, but it is the very first project that I started with ketogenic therapies, right? So, when we think about Alzheimer's disease, classically we think about our genetic destiny, is to have Alzheimer's if our parents had it, or our grandparents had it or something like that. But we are... We can be genetically predisposed to having Alzheimer's disease, but it's a very... Genes really drive maybe 5% of Alzheimer's.

SHAWN STEVENSON: In the upper end.

DR. DOMINIC D'AGOSTINO: Yeah. Yeah. Yeah, that's being... Some people will say 2% or 1% or... If you're APOE4 positive, for example. But we know that prevention strategies will probably have the biggest impact on this. So, whatever's good for our heart is good for our brains. So, our metabolic... Our overall metabolic health will be a huge factor in influencing metabolic biomarkers that are tightly coupled to not only cardiovascular health, but whatever's good for the heart is good for the brain, so brain health too. So that is things like keeping your blood sugar in check, keeping inflammation low, telling the doctor, "Hey, I... In addition to your CBC and CMP blood work, your Comprehensive Metabolic Panel, to throw in insulin." I don't know, for some reason we don't measure insulin. Throw in a simple measure of systemic

inflammation like HSCRP, high-sensitivity C-reactive protein. These two things alone coupled with glucose are... Can be very important predictors of not only our metabolic health but our trajectory of getting age-related chronic diseases, including Alzheimer's disease. So, this is... Upfront, this a very important thing that people should know. Metabolic health will predict us getting age-related dementias, including in that Alzheimer's disease.

So, a hallmark characteristic of Alzheimer's disease is glucose hypometabolism. Meaning that if you scan someone who has advanced Alzheimer's disease or even early dementia, what you see in a fluoro-deoxyglucose PET scan, an FDG PET scan, which is a technology that can be used to look at the location and aggressiveness of tumors, but we can also image the brain, and it shows brain glucose uptake. In people with Alzheimer's disease, it's far less lit up, so it's much dimmer. So, it's basically indicating that there's glucose hypometabolism. And the reason for that is largely unknown. And I think it's important to state right up front that the etiology of epilep... Of Alzheimer's disease and other diseases that we study like epilepsy is largely unknown, right? So, there could be multi-faceted or multi-factorial things contributing to Alzheimer's disease, but a hallmark characteristic is impaired energy production. So, brain energy is impaired, and no one would dispute that. The reason that we have in paired glucose metabolism in the brain is there could be a wide variety of reasons. It could be the vasculature and the arteries that feed the brain energy, oxygenated blood, and glucose, are impaired. There's a vascular component.

There's also... We transport glucose into the brain through two different ways. At the blood-brain barrier, you have the GLUT1 transporter, and at the level of the mitochondria and the cell itself, the neurons, is the GLUT3 transporter. And then once the glucose gets into the cell to be used by the mitochondria to make ATP, ATP is the energy currency of the cell, that we need an enzyme called pyruvate dehydrogenase complex.

So, taking a step back, we know that it could be a combination of a decreased brain energy just through brain blood flow. So, it's very common, people who have Alzheimer's disease, have a decrease in brain blood flow, it's very common for them to have... If you look at the GLUT3 transporter on the surface of the neurons, these tend to be internalized, so you have a cell membrane with a GLUT3 transporter, and that transporter can be inactive, or it can be internalized inside the cell so the glucose can't get in. And then, once the glucose is in the cell, it requires pyruvate dehydrogenase complex, which is the gatekeeper and the rate-limiting enzyme for glucose oxidation. And that...

SHAWN STEVENSON: To make ATP.

DR. DOMINIC D'AGOSTINO: Yes, and there are the tons of papers you can look at a PDH complex and Alzheimer disease that another hallmark characteristic is a reduction in the PDH enzyme

and also in the total enzyme protein, but also a reduction in the catalytic activity of that protein. So even if we make it, it's not as active. So, taking a step back, this is actually what got me interested in using a ketogenic metabolic therapy, nutritional therapy for Alzheimer's disease. So, it was clear in the literature that elevating ketones through fasting through the Ketogenic diet or even exogenous ketones can elevate brain blood flow by 30% or more, simply fasting for 24 hours and the naive subjects actually increases... You can do a Doppler blood flow measurement, and blood flow to the brain increases by 30%. And you could say, well, because you have less blood in the digestive organs, digesting food and things like that, so that could be it, but what's actually happening is that you have more blood in the reserves because you're not digesting the blood is not in internal organs, but what also happens is that the ketone bodies actually stimulate adenosine. Adenosine is a vasodilator, and it increases brain blood flow.

So, transitioning away from a carbohydrate-based standard American diet to a state of ketosis will increase brain blood flow. The ketones bypass the glucose transporters. So, for example, in glucose transporter type 1 deficiency syndrome, which is a genetic inborn error metabolism, the therapy is actually ketosis, the ketogenic diet, because the ketones then replace glucose as the primary fuel for the brain.

So, in Alzheimer's disease, you have impaired glucose transport by virtue of a reduction in brain blood flow, maybe a decrease of glucose across the blood-brain barrier, but very likely a decrease in glucose uptake into the neurons that is a result of an internalized GLUT3 transporter or an inactive and a decrease in the total amount of pyruvate dehydrogenase complex and the catalytic activity of that enzyme is decreased. All of these things that I just mentioned, which basically encompass the hallmarks of Alzheimer disease, can be overcome in a state of therapeutic ketosis. So, with therapeutic ketosis, your blood glucose levels remain stable, the homeostatic mechanisms that maintain our blood glucose are very strong. So, when you eliminate all sugar and carbohydrates, your glucose does not go to zero, it will stay in the low normal range, but our ketones are elevated, and we know that the ketones can largely replace or supplement glucose as a primary energy source for the brain. So, as we age, our brain has impaired glucose metabolism. Work done by Stephen Cunnane, for example, and others have demonstrated that as we age, the brain's ability to use ketones is maintained. So, essentially, what that means is that if we...

SHAWN STEVENSON: While glucose goes down.

DR. DOMINIC D'AGOSTINO: Yes, while glucose goes down, because at the level of the neuron in the mitochondria, there are many more steps required to oxidize glucose for energy, ATP, than are required to oxidize ketone bodies for energy to make ATP. So that's why, if you have pyruvate dehydrogenase complex deficiency syndrome or GLUT1 deficiency syndrome, the

standard of care that we use, it's not an alternative therapy, the standard of care that we use is a ketogenic diet because it bypasses the glucose dysregulation to supply the brain with energy and restore brain energy metabolism. But it's not only restoring brain energy metabolism, when you re-store metabolism, you're also restoring the balance of neurotransmitters, you're also decreasing neuro inflammation, there are many energy-dependent processes in the brain that function to keep the brain healthy included in that... And I put this towards the end because I think it's a downstream epiphenomenon, included in that is the accumulation of amyloid beta and tau plaques. So we are of the opinion that the etiology of Alzheimer's is incredibly complex, but there's without a doubt a metabolic component.

So, Dr. Mary Newport is someone who got me interested in this, and we are talking about her prior... And her book comes out, I think in November called Keto Clarity, I believe, and I wrote the foreword to the book, just to plug Dr. Newport's book, but There was a news article in the St. Pete Times, I'm trying to remember the day, 2007 or 2008, and it was the observation that giving her husband MCT oil and coconut oil together improved his performance in the mini-mental state exam and also the clock test. He was being evaluated at the Byrd Alzheimer's Institute at University of South Florida College of Medicine. And this made local news and then it made national news, and then this is just when I was just getting interested in ketones as neuroprotective agents for Navy SEAL divers. So, I saw that, hey, you could elevate ketones in the blood independent of diet by giving MCT and coconut oil. So, Mary and I connected, long story short, it led to a PhD project who now, Dr. Milene Brownlow, she did her PhD at the Alzheimer Institute on a mouse model of Alzheimer's disease, which is tau and amyloid plaques. So, these mouse models of Alzheimer's disease are not that great.

So, when people look at pre-clinical animal model research, you have to view it with a grain of salt. Nonetheless, we saw a nice effect. In particular, we saw effect that the mice ran faster and farther on a rotor-rod device, which is like a treadmill kind of like device. So... And an... A really important problem with Alzheimer's disease is impaired motor function, impaired stability. They fall, they lose their function, their independence, and that's a downstream slope. So, we saw very nice effects across the board, but not so much on tau and amyloid when you start the metabolic therapy late, at least in a mouse model. But Dr. Dale Bredesen, and you could just go to his book or maybe have him on your podcast, he's done a lot of work in patients using similar approaches, ketogenic metabolic therapy. So that was a long-winded way to say that Alzheimer's disease, the etiology is largely unknown in the medical literature, but there's a tremendous metabolic component. The... And the hallmark characteristics is impaired glucose metabolism, being in a state of therapeutic ketosis, that can be achieved with time-restricted feeding, that can be achieved with ketogenic diets.

I'm in favor of a modified Mediterranean-style ketogenic diet that we can talk about, or you can use supplemental ketogenic agents, like medium-chain triglycerides, ketone salts or ketone esters can be used, or a combination of all these things, to target brain energy metabolism. And Alzheimer's disease is characterized by the accumulation of amyloid plaque. So, we think that that's more of a downstream epiphenomenon of the neuroinflammation of the impaired energy metabolism and the associated cascade of events that are associated with just an impairment of metabolic function in the brain.

SHAWN STEVENSON: Yeah. Thank you for breaking that down. Because when we hear impaired glucose metabolism, we don't really know what that means, and there's different levels to it. And so having an alternative fuel source essentially that's able to bypass some of these processes that are dependent upon glucose is really important. Because as you know, one of the blanket labels getting thrown on Alzheimer's now is Type 3 diabetes.

DR. DOMINIC D'AGOSTINO: Oh yeah, yeah.

SHAWN STEVENSON: That's kind of impaired glucose metabolism, but also sort of like an insulin resistance taking place in the brain itself. And this issue has... Of course, has been growing and going and growing. And I love the fact that you said the etiology itself is... It's complex, not exactly... We don't have a finger on it, but we know, we know this has a lot to do with our diet, our sugar intake. But also, if we're talking about the build-up of these kind of metabolic wastes and amyloid plaques and things of that nature, we've got systems that help to clean house in the brain for example that can get impaired from sleep deprivation.

DR. DOMINIC D'AGOSTINO: Yeah. Oh sleep, I think another thing... Yeah. Mm-hmm.

SHAWN STEVENSON: So, researchers... I think it was at University of Rochester...

DR. DOMINIC D'AGOSTINO: Yeah.

SHAWN STEVENSON: They found that like the glymphatic system that helps to clean out these metabolic wastes is 10 times more active, upwards of 10 times more active when we're sleeping than when we're awake. And guess what another one of our epidemics is? Is sleep deprivation in our society today.

DR. DOMINIC D'AGOSTINO: Major contributor. Glad you brought that up. Yeah, 'cause sleep is highly correlated with neuro-inflammation in the brain and even gut... You miss a night of sleep, and it's going to make your... We're talking about zonulin being activated. That's a protein that's associated with the tight junctions, it maintains... When it's released, it can cause leaky gut just by increasing paracellular transport across the intestinal epithelial lining but also

the blood-brain barrier. One night of sleep, one... If you're thrown into a situation where you have acute stress, and epinephrine goes up, and cortisol goes up, you can trigger injury, infection, inflammation, diet, all these things impact zonulin, which is classically associated with the gut permeability, but we have those same tight junctions in our blood-brain barrier. And once that's compromised, you're releasing things into circulation, things that we study in the lab, like lipopolysaccharide or LPS.

And these can cause... Like sometimes people will have a traumatic event or give a big talk, and shortly after... Or travel to a location, come back, and then they get a headache the next day. That headache is likely gut inflammation, which contributes to inflammation and permeability of the blood-brain barrier, letting things into your brain, triggering a low-grade inflammation. And that can then trigger things like Epstein-Barr Virus or herpes simplex Virus or shingles or things like that. And then that can trigger an event that people have. But that's why we really focus on stress resilience. So, making the body... Implementing metabolic-based therapies and other strategies to make the body more resilient in the context of these stressors. So the stressors that we study are extreme environments, the undersea environment, the altitude environment and the space environment. And then also what we call being task-loaded, so we do a variety of psychological measures to understand why and how people get stressed and how to mitigate that.

SHAWN STEVENSON: Yeah. And your research isn't just theoretical, you are actually spending time under water. Can you talk a little bit about that, because you just blew my mind when you shared it before the show?

DR. DOMINIC D'AGOSTINO: Yeah, yeah. Thanks. Yeah, my research started doing... Just taking a little bit of step back quickly, patch-clamp electrophysiology on neurons when I did my PhD, right? So that's a very... You're looking at cells, individual cells. Then it led to animals, and then it led... Well, then it led to tissues, and then animal models, and then human clinical trials, and then ultimately what we call operational experiments, where we are the subjects on an IRB-approved study by a federal agency. And in this case, it was NASA's Extreme Environment Mission Operations or NEEMO, N-E-E-M-O. So, I was on NEEMO 22, and my wife was on an all-female crew of NEEMO 23. So, NASA uses an underwater habitat called the Aquarius habitat, which is off the Keys in Florida. And they bring astronauts to these habitats to train them on a variety of different things, including different operational activities that NASA has. It could be devices that are used underwater in the underwater habitat.

So basically tools, techniques, procedures, and things are vetted out and tested in the space analog, what's called a space analog habitat. And there's... NASA has quite a bit of... They got at least a dozen space analogs. HI-SEAS is one. We're involved in some of that, here emissions. But the NEEMO, NASA's Extreme Environment Mission Operations, is really the only space

training facility that actually uses astronauts. And three of those astronauts are on ISS now. Kjell Lindgren, Samantha Cristoforetti is at ESA, Italian astronaut, and Jessica Watkins.

SHAWN STEVENSON: So, they're on the International Space Station right now.

DR. DOMINIC D'AGOSTINO: They're on the International Space Station now. Yeah. They flew up in SpaceX Crew-4, which launched a few months ago. We actually went to the launch and got to meet them before, 'cause we spent a lot of time training with them at NASA, but also inside the habitat under water for 10 days. Under water. Yeah.

SHAWN STEVENSON: Wait, wait, wait. Say it again. You spent 10 days under water.

DR. DOMINIC D'AGOSTINO: 10 days underwater in the Aquarius habitat for NEEMO 22 was my mission. That was back in 2017. And when you live under water at... We're at three atmospheres.

SHAWN STEVENSON: Wait, wait. Just can you hear yourself right now, Dom? When you live under water, that's not a normal thing to say.

DR. DOMINIC D'AGOSTINO: Yeah. You become an aquanaut. And I think there was about 60 or 70 astronauts. Most astronauts in training now have to do this mission as part of their training. In 24 hours under water, you become an aquanaut. And that basically means when you go recreational scuba diving, you dive under and then you have to come up in a pre-determined amount of time according to the no-decompression limits. So, you don't want to have to go into a hyperbaric chamber, or you can die. So, if you're under water and at 100 feet and you stay down for three hours and shoot up to the surface, you're going to die a very painful death from decompression sickness, it's also called the bends. When you live under water, you are living in a state which is called saturation. So, you're breathing in the gases, and those gases equilibrate with your body, so your body is retaining a lot of nitrogen and a lot of oxygen. And it's also the CO2 concentration, we're breathing 300, or now it's a little bit higher, 400 parts per million of CO2 now, but in the habitat of the International Space Station or in this space training analog, it's about 3000 to sometimes it went up to 8000 parts per million of CO2. And that's considered hypercapnia.

And when CO2 levels rise, it equilibrates with your body, and it actually hits these tight junctions and makes your leaky gut. And I tested my urine for neurotransmitters, my blood, my saliva, I looked at the hormones, and the thing that jumped out is oxidative stress goes way up, and my C-reactive protein, which is always like 0.1 or non-detectable went up to like 6.5 or something like that. That's because these extreme environments impact things like the gut microbiome and the integrity of the epithelial lining of the gut, but also the blood-brain

barrier. So, we have to understand what happens when you put people in these artificial habitats, and you could say, in office is like an artificial habitat, with elevated partial pressure of these breathing gases, because we have to send people to Mars and back and bring them home safely, we need to create countermeasures to enhance their safety and resilience and performance in these extreme environments. And that's a big part of what we do in our lab, but also outside of the lab. In collaboration with Duke, we have some studies too, but also, as test subjects ourselves, and also principal investigators on various things, we vet out different procedures. And something that we think is very important is optimizing our physiology to improve our brain resilience and our overall longevity in these extreme environments, which are very pro-oxidative, pro-inflammatory.

SHAWN STEVENSON: This is so fascinating. And this is... There's two things here. It speaks really to the resilience and adaptability of humans, and also, when we think about these extreme environments, we're talking about this kind of external environment, and even now we're in this kind of artificial, put together scenery, setting. And the thing is, even as I say that I realize that we are part of nature as humans, and the stuff that we create is still nature. But when we start to pull away from our... The circadian patterns and all these different things, we start to alter what our genes are doing, which we talked about before we got started too. So, I want to circle back and talk about genes in a moment. But the extreme environments, we're thinking about externally. But what we're also doing as a culture is creating these extreme environments internally with our food, for example. And then we can have external manifestations of that, which for you was eczema, was something that you...

DR. DOMINIC D'AGOSTINO: That's right. Yeah.

SHAWN STEVENSON: Struggled with for a long time. Can you talk about that and how you solved it?

DR. DOMINIC D'AGOSTINO: Yeah. Yeah. Yeah, yeah. Yeah, that actually brought me to the field of nutrition. I was not a good student. I was in classes that were... That they put the dumb kids in, kind of grow... At a very young age. And then as I got increasingly interested in biology, I was doing a little bit better, and then in high school, took college Biology. And by the time I finished college, I was a fairly good student, but not great. But because I got very interested in biology because I wanted to enhance my strength and working out and nutrition, and that was a big aspect of it, but I learned that as I changed my nutrition, my eczema, which is something that I dealt with for many years, in a few case, I remember playing football where the eczema got irritated and it led to something called impetigo, which was like a staph infection and stuff. And this happened a couple times. And it was just, no matter what creams... If I used corticosteroids and put them on, they would work for just a week or two, and then they would

have this rebound effect. Then they would stop working, then I would stop using it, and then it was worse than when I was using the steroids.

So, I struggled with this constantly until I started studying nutrition. And I think it was Barry Sears came out with a book in the early '90s called The Zone Diet. And then I started reading a little bit more about this, and I majored in Nutrition as an undergrad, and I just simply removed processed grains, and was just... Went from a lot of pasta and bread, I grew up in an Italian family, and we... Who still eats pasta, but I phased that out and kind of replaced it with sweet potatoes and brown rice and things. And then it got tremendously better. I started eating more fish and fish oils.

And then occasional I'd reintroduce grains and other things back in and bam, the eczema would come back. Like within about a week or two, so I repeated this experiment a couple of times, if you want to call it an experiment, and it validated in my mind that this was a trigger, but this is before I knew anything about zonulin and glyodin and all the factors that could be influencing the immune system, the gut and the immune system. So that sparked my interest in addition to the fitness, being very interested in fitness and weightlifting into how nutrition could be used to treat an autoimmune.

I became a believer even before people were talking about using nutrition to attenuate or even completely abolish autoimmune disorders, and that set me on a path for thinking about nutrition as the primary lever to pull for our overall health, not just... Metabolic health is tied to brain health, cardiovascular health, and everything in between. So, as I went down the nutrition path, I wanted to go to medical school, and I saw... I thought the general consensus was that nutrition was kind of like a soft science.

So, I double-majored in biology too to get that under my belt, and then the '90s was the decade of the brain, so I got steered into a neuroscience and physiology program instead of a nutrition program. I'm glad I did because I think it was a little bit more rigorous at the time, although if I was to go back in time. If I was to go back into college now, I'd probably study nutrition and just study nutrition, I would study nutrition and neuroscience on the side instead of neuroscience and nutrition on the side.

But when I would go to national conferences like Experimental Biology or Society for Neuroscience, I would gravitate right to the nutrition stuff, so experimental biology, I was a physiologist, but I would actually look to see, "Hey, what's on the nutrition, what's being presented." And I would go to all the nutrition things. So, I had this passion for nutrition, and then ultimately, my post-doctoral fellowship was basically designing nutritional strategies for oxygen toxicity seizures, which are limitation for Navy SEAL divers, when they use a closed-circuit rebreather.

And that ties into our underwater mission with NASA. But yeah, that was a little bit of the circuitous theme, but it really... I think it may have started with the eczema because I was reading at the time Muscle & Fitness and other things. And I'd always read the little nutrition things here and there, and it was giving me clues that nutrition was a major player in our skin health and our immune health and things like that, and then overall inflammation.

So, Barry Sears' book talked about eicosanoids and prostaglandins and how to engineer your diet to reverse this pro-inflammatory state, and that was really the steppingstone for me. And then I would talk to my professors in nutrition about this, and they kind of rolled her eyes because there wasn't really a favorable outlook, it was always about low fat, keep fat as low as possible, keep the carbs high, healthy whole grains.

SHAWN STEVENSON: Yeah, I had the same experience, of course, going to conventional university, but this speaks also... Your story speaks to the power of our psychology now that influences our results, because for somebody to hear coming into this that you were a poor student at some point when you are one of the foremost brilliant thinkers in this field today, it's just really remarkable, but you got tied into that because of a passion, because of an interest, because of a real world effect for you, and you kind of fleshed out your inherent genius through that experience and I want to ask you about this, because...

DR. DOMINIC D'AGOSTINO: Absolutely. It's like your experience too, you immerse yourself and you can't manufacture enthusiasm, so you need to be limbically, emotionally, motivated on a subject to really do your best, otherwise you're just kind of manufacturing enthusiasm, it's only going to take you so far, but you have... That's why I tell my students, it's like, "Well, they could have the best CV or a resume in the world," but I was like, "Well, I try to find out what internally motivates them and then put them in that position. So, I think that's what led to it, I found out what I was very interested in.

SHAWN STEVENSON: Here's the rub, there is this really interesting interaction that I don't know if you've really thought about this, because you have that passion piece, but then you actually start to feel better, you start to get results in the real world. And when you marry those two things together, it's remarkable what happens, and this leads into this conversation today about mental health, just being able to actually do some of the things that we're talking about, and it's...

When we start looking at some of the statistics right now, it's mind-blowing, the leading cause of death right now currently for people between the ages of 18 and 45 is drug overdose right here in the United States. And people don't... We see that and we think, of course, we have this tendency, this bias of like, "Oh, it's just these drug users, this kind of thing." And we fail to

realize what are the underlying mechanisms that drive people towards this behavior? Oftentimes, they are trying to self-medicate or medicate through the collective agreement with their physician as well, because even with Fentanyl, that's the number one killer by the way.

When I say a drug overdose, specifically from Fentanyl, right? And so, we're medicating, we're dealing with pain. Physiological, psychological pain, that we're trying to address. So, what I want to ask you about is how your work and even ketogenic diet plays into helping to address our mental health, because I think a big driver, just one of those foundational things behind our struggles with mental health, anxiety, depression, ADHD has a lot to do with our diet.

DR. DOMINIC D'AGOSTINO: Yeah, I'm glad you brought that up in a nice segue from kind of following your passion, because when you follow a nutrition program, not only does it change your physiology, but that physiology changes your mental state. And that's... I became very interested in this idea, which was brought to me by... A couple people were key influencers that... More academics, not influencers in the conventional, modern-day social media sense. But they influenced me to an amazing degree. Dr. Jong Rho, he did a lot of work showing that ketogenic diet can change your metabolic physiology, which changes your brain neuropharmacology. So that work led me... It's actually email communication through him that I sent to a DO... Department of Defense program manager that ultimately ended up in my funding. So, it was...

He changed my mind on that, that... And also, there was a patient in the UK that had epilepsy, and his name is Mike Dancer. And if you Google, Mike Dancer epilepsy, you come up with a very interesting story, and he was sort of in the fitness world too. And the ketogenic diet not only controlled the seizures, it significantly improved his mental health. And I realized I could see that just from the back end, that the ketogenic diet was an effective metabolic therapy that had good science behind it for 100 years now, and that it was doing it by changing the neuropharmacology of the brain in a way that changes neurotransmitter systems. For exam... Gluta... More glutamate is converted to GABA, and GABA-ergic drugs, as you know, benzodiazepines, Valium, Xanax, these are anti-anxiety drugs, right? And we've seen this in our experimental models too, that if you induce a state of therapeutic ketosis, and that could be with fasting, that could be with a ketogenic diet, or it could be with supplemental ketones to elevate ketone levels in the blood and in the brain. But there's a greater activation of an enzyme, GAD 65 and 67, I think, that convert... This is glutamic acid decarboxylase, that's how we make neurotransmitters.

So, we make glutamate from alpha-ketoglutamate... Glutarate. And then the glutamate then becomes GABA. Glutamate is an excitatory neurotransmitter. And when we have epilepsy, when we have Parkinson's, Alzheimer's disease, traumatic brain injury, we have an excess of

glutamate in the brain, and that causes hyperexcitability and neurotoxicity in the brain. So, what the ketogenic diet does is it balances... And this is just one neurotransmitter system, but it does it to multiple systems. It converts more of that glutamate, which is hyper excitatory, to GABA, which is very calming. So that's why Vigabatrin, for example, is an anti-epilepsy drug. The benzodiazepines hit the GABA receptor, GABA1 receptor, the GABA A. So, in doing so, it became very apparent to me that the ketogenic diet was a legitimate medical therapy for epilepsy. Controlled studies by Mayo Clinic, Johns Hopkins, specifically, Dr. Eric Kossoff and Mackenzie Cervenka are leading the way. They were mentored by the late John Freeman, who really spearheaded the use of the ketogenic diet at Johns Hopkins to develop that neurology ketogenic diet program there. And so... And then there was a movie about the ketogenic diet by Meryl Streep, and that really led to advance the visibility of the Charlie Foundation with Jim Abrahams, who's here in Hollywood, he lives. And he inspired me and incorporated Jim into the TEDx talk that I gave a long time ago. But it was really...

I knew in the back of my mind that the ketogenic diet was... It's the only diet... There's no other diet that you can follow that actually stops epilepsy. You can... If you do a Mediterranean diet, a low-fat diet or any other diet and even reduce calories, create a caloric deficit, it does not change brain neurotransmitter systems to control seizures. So, the ketogenic diet does that, and that's a very unique feature, and that's what makes it in metabolic therapy. So, in many cases where you have psychiatric disorders, and this is sort of the segue to brain health, or a mental state... When you have a psychiatric disorder, like bipolar for example, patients are often put on anti-epileptic drugs to control the manic episode, to control various aspects of psychiatric illnesses. And it kind of made sense. And this is sort of further validated by the work of Chris Palmer at Harvard and Dr. Shebani Sethi at Stanford, who really coined the term, "metabolic psychiatry." And there's a big movement right now being spearheaded and funded by Jan and David Baszucki that is basically putting funds towards answering this question, "Does nutritional therapies like the ketogenic diet as a metabolic therapy change brain energy metabolism and neurotransmitter systems to basically advance this entire field of psychiatry?" And to give...

Because psychiatric drugs are not working in many cases. Bipolar, schizophrenia, depression, these things are very complex disorders. The etiology of these things are largely unknown. With schizophrenia, there's a genetic component, but not so much with bi... Not a whole lot with depression. But other things, there's a genetic component. So, we know that neurotransmitter systems are being hit by ketogenic diet therapies and through brain energy metabolism, through the gut microbiome, through reducing neuroinflammation and just by changing and losing weight. If you have patients... And in this case, if you have... You could use any diet and take someone who has depression, anxiety, schizophrenia and get them to lose weight.

It's going to change metabolic biomarkers like insulin, glucose, inflammation, and other things that would improve their psychological state and how they feel about themselves. But the advantage of using the ketogenic diet is that it has a much more profound effect at changing the brain chemistry and stabilizing neurotransmission in a way that has particular efficacy at controlling the manic episodes associated with bipolar, and probably the depressive episodes too. So, there's a big movement being spearheaded right now by the Baszucki brain research fund in large part through the efforts of Dr. Christopher Palmer, who has a book coming out in November called Brain Energy. I have an advanced copy of that, and it's great, I think you should have him on.

So, he's really advancing this is a number of investigators, there's a big group that's expanding very rapidly. There's about two dozen people involved in this group, including Dr. Jeff Volek at Ohio State University. Who's been doing ketogenic therapies before when I was even in grad school and didn't even know the ketogenic diet was sort of used outside of the world of epilepsy. So keep your eye on this field of metabolic psychiatry, and I think that once the research is conducted and published and accepted, we will have a very powerful tool in the tool box that will be hopefully embraced by the medical community, by psychiatrists who maybe rebrand themselves as metabolic psychiatrists, because this is a rapidly expanding field in research, thanks to some generous funding organizations through the Baszuckis, who are supporting an aspect of our clinical trial using continuous glucose monitors and to look at metabolic optimization and a component of that study that is also being spearheaded with partnership with the Dr. Allison Hull of Florida Medical Clinic. We are looking at mood, we are looking at sleep, we are looking at various aspects of mental health by putting continuous glucose monitors on patients and coupling that with a low-carb ketogenic diet and non-diabetic patients.

So just taking the average everyday person who does not necessarily have diabetes or any over-medical condition and optimizing their nutrition, putting a wearable device on them as a behavioral tool, and then looking at not only a whole bunch of metabolic cardio metabolic biomarkers, but also looking at your psychiatric biomarkers and mental state. So, we think that the data coming out of that right now is not published, we've published it in abstract form, but we're analyzing a lot of the data now, but for one thing that really jumped out was non-alcoholic fatty liver disease. So, patients who are not obese, patients who did not have type 2 diabetes, when you put them on a low-carb diet, that it reversed their hepatic steatosis, which is fatty liver. But what was really surprising is that they did not know they had fatty liver disease until we scanned them because it doesn't show up in the liver enzymes. And that's an ALT may be slightly elevated and that's like an early, but once your liver enzymes are above and outside the normal range, then you already, you're getting fibrosis in the liver.

SHAWN STEVENSON: Right, right it's too late.

DR. DOMINIC D'AGOSTINO: So, it's like hard to reverse. Yeah, so you have to do, we tried to propose a CT scan, but that's radiation and the IRB didn't like it, so we got a team that does very high-resolution ultrasound and we could image, and people thought they were totally fine. They didn't have diabetes, they didn't have any kind of irregularities, but they had fatty liver, and the precursors to a potential fibrotic fatty liver that would be potentially irreversible.

SHAWN STEVENSON: It's another one of those hidden epidemics' fatty liver.

DR. DOMINIC D'AGOSTINO: Yeah, it is.

SHAWN STEVENSON: And also, you've mentioned neuro inflammation several times, there's some things that until we actually see symptoms, it's so far gone. But you mentioned this continuous glucose monitor and also you mentioned someone at the Ohio State University as well. And it reminds me of a study because with the ketogenic approach, we have a viable tool for improving mental health through that lens of, as you mentioned, changing neurochemistry but also simply stabilizing blood sugar because that is one of those right now in the United States, we're knocking on the door of about 130 million citizens have type 2 diabetes or pre-diabetes right now. So chronic issues with blood sugar regulation. And there was a study that was done at the Ohio State University on married couples. And what they did was they gave them some devices to monitor their glucose and the scientists were able to track this and stay on top of their data. And throughout the day, what they found was that when couples blood sugar was dysregulated, they were more likely to have arguments with their spouse. And here at the end of the study, they were far less likely to resolve their relationship conflicts when their blood sugar was dysregulated and dysfunctional. Right.

DR. DOMINIC D'AGOSTINO: Yeah, yeah.

SHAWN STEVENSON: So again, we have another tool here to supplant, because it's not just the fact of the ketogenic approach helping with the neurochemistry, it's pulling out that major culprit, which is ultra-processed foods, likely high in sugar and high in ultra-processed carbohydrates as well.

DR. DOMINIC D'AGOSTINO: Absolutely, and I was just talking, I was telling you, I'm at the Ancestral Health Symposium and Dr. Robert Lustig, has a lot of insight in this and a lot of experience in treating patients and everything. And that's really like, I think the low-hanging fruit, especially sugar-laden beverages, which are essentially giving the body, it's a liquid candy, and it's like giving the body an IV bolus of glucose really. Actually, it would be less dangerous giving an IV bolus of glucose because you'd have a less of an insulin response, but when that bolus of glucose hits the gut, it's immediately absorbed and enter circulation and has a

profound effect on our gut hormones. Not only our gut hormones but the neuronal circuitry associated with eating behaviors and triggering, for example, a dump in dopamine, which you're going to then go seek more dopamine when you spike dopamine through these repeated glucose boluses. So, not only it's just an empty calorie, but it's actually the how these things affect brain chemistry and gut microbiome and things like that.

So, this has to be recognized, and he's done a lot of work. So, sugar delivered in the form of a liquid bolus is much more atherogenic, causes much more metabolic damage than sugar delivered in processed food. They're both terrible, but the sugar delivered in a liquid bolus is on the order of magnitude of almost double of what you get depending on the food that it's incorporated into, just because of the metabolic response that's associated with consuming a liquid bolus of sugar. And that's really the low hanging fruit. I think we just need to educate people around that, but you go into impoverished communities, and that's all you see on the shelves it's all people are buying, 'cause it's cheaper than the water, right? So, you go to areas where we've done sort of education camps like West Virginia, or like parts of Appalachia, for example and that's all they drink is just Mountain Dew and Coke and things like that. And they give it to their babies, instead of formula. And that's like... That's causing diabetes in infants before they even have a chance in life. And that's really heartbreaking.

SHAWN STEVENSON: This is not a joke. I've seen this in baby bottles in my family...

DR. DOMINIC D'AGOSTINO: Oh, really in your family.

SHAWN STEVENSON: Of course, yeah.

DR. DOMINIC D'AGOSTINO: Wow.

SHAWN STEVENSON: Like one of the first things that we do, like when a baby can hold on to a McDonald's french fry... You know what I mean?

DR. DOMINIC D'AGOSTINO: Yeah, yeah.

SHAWN STEVENSON: And it's just a part of the culture. We don't realize that food has these impacts. And yet we have 90% of family members having some form of chronic disease and upwards of 80% to 90% being obese. But we don't realize this is a thing about exposure and making information like yours accessible and just the frameworks of eating. We've got a quick break coming up. We'll be right back.

Our microbiome plays major roles in regulating our metabolism. Literally playing a role in determining how many calories are absorbed from our food, for example. Our microbiome

also controls so much about our mood with the vast majority of our body serotonin being produced in our gut. And our microbes interact with these enterochromaffin cells and enteroendocrine cells that produce our hormones and neurotransmitters in our bellies.

And one of the biggest issues we're seeing today is gut dysbiosis, where friendly microbes are getting overrun by opportunistic bacteria. One of the few amazing sources of nutrition that's been found clinically to reverse gut dysbiosis is highlighted in a study published in the Journal of Agricultural and Food Chemistry.

It discovered that the traditional fermented tea called pu'er may be able to reverse dysbiosis by dramatically reducing ratios of potentially harmful bacteria and increasing ratios of beneficial bacteria. Another peer reviewed study published in the journal, Nature Communications, uncovered that a unique compound called theabrownin found in traditional fermented pu'er has remarkable effects on our microbiome as well.

And the researchers found that deal theabrownin positively alters gut microbiota and directly reduces hepatic AKA liver fat and reduces lipogenesis, which means the creation of fat. Pu'er is absolutely amazing on so many levels, and it's also a powerful adjunct to any fat loss protocol because it's been found to support fat loss while protecting muscle at the same time. And this was documented in a recent study featured in Clinical Interventions in Aging.

Now, the key is the source of the pu'er matters a lot. And the only pu'er that I drink, uses a patented cold extraction technology that extracts the bioactive compounds in the tea at cold to low temperatures for up to eight hours. And this process gently extracts natural antioxidants and phytonutrients and preserves them in a whole bio available form. And this is the purest way to extract the phytonutrients for maximum efficacy.

This pu'er is also wild harvested, making it even more concentrated in the polyphenols that we see having benefits in those clinical trials. Also, triple toxin screened for one of the highest levels of purity. Tested for pesticides, heavy metals, and toxic mold, and making sure that it is not in your tea, which is common in most other teas. This is why I'm a massive fan of Pique Teas. Go to piquetea.com/model. That's P-I-Q-U-E-T-E-A.com/model and you get 10% off their amazing fermented pu'er and all of their other incredible teas. These teas are in a league of their own. Their pu'er is amazing. I'm a huge fan of their ginger tea as well. Go to piquetea.com/model. Again, you get 10% off, everything that they carry. One of the best investments in your health supporting your microbiome, supporting your metabolism, it is absolutely amazing. Head over to piquetea.com/model. And now back to the show.

One of the things I really enjoy about ketogenic approach is the fact that it gives a framework. So, you know that these things are not a part of this. And it's just that in of itself is so nourishing

and healing versus just trying to micromanage calories while still including these processed foods or... Like soda and things like this. Just that one action of taking out this liquid barrage of sugar can be so changing for our metabolism...

DR. DOMINIC D'AGOSTINO: Huge.

SHAWN STEVENSON: For our brain. The list goes on and on. And I want to ask you about this because we've circled around this several times.

DR. DOMINIC D'AGOSTINO: Okay.

SHAWN STEVENSON: It was researchers at Albert Einstein College of Medicine, they published some really fascinating data recently, and they were looking at neuroinflammation. And they felt that it was a double-edged sword of nutritional diseases that... Our epidemics of neuroinflammation is contributing to insulin resistance and obesity specifically adiposity of the gut. And adiposity of the gut, insulin resistance was creating more neuroinflammation. So having excessive body fat was creating inflammation in the brain... It's creating this vicious circle.

And people might think, "Well, how do I know if my brain is inflamed?" It's like our brain is so protective and not particularly having even pain receptors in the brain itself... Because the brain is responsible for telling you and managing pain in other parts of the body. But when the brain is hurting, we often don't know until it's too late. So, let's talk a little bit about neuroinflammation and how it's... We've touched on a little bit how it's being created, but what are some of the things we can do to reduce this neuroinflammation?

DR. DOMINIC D'AGOSTINO: Yeah, so you talked about adipose tissue causing inflammation and we know that... One thing that comes to mind is that adipose tissue is an endocrine organ. When I was in nutrition, studying in the '90s, we didn't talk about our fat being an endocrine organ, releasing adiponectin, and of course, leptin. As we lose weight and we get super lean, then our leptin goes down proportionally. And that sort of can factor and trigger other things and influence things like neuropeptide y and ghrelin that cause us to eat again. But that's why everybody has a set point. But I think that set point can be changed. But getting back to this theme of neuroinflammation and adipose, the best thing to do to reduce neuroinflammation is, really, to focus on... And I don't want to sound overly simplistic, but basically doing a nutritional and exercise approach, 'cause I think nutrition needs to be coupled with exercise for maximum to alter body composition.

So, as we get a more favorable body composition alterations through a nutritional intervention, it doesn't have to be a ketogenic diet, it could be, ideally, like with older people,

high protein, moderate fat, high fiber. So instead of low carb, I like to say high fiber. So just incorporating fibrous carbs, like vegetables. And I know there's a little bit of a backlash maybe in the carnivore community about eating vegetables and things like that, but I definitely think you would have a very hard time arguing about the benefits of fiber. There's just so much information on that. So, first things first, is just optimize, focus on optimizing metabolic biomarkers, and that would be your glucose levels, your insulin levels, which you should request getting measured, and also request, simply, a marker of inflammation, high-sensitivity C-reactive protein. Systemic inflammation is tightly coupled to neuroinflammation if you have inflammation throughout your body. And you don't have to do a full Cytokine/Chemokine panel, but I think high-sensitivity C-reactive protein is really core. The more data... I used to think very loosely about this, oh, it's just a non-specific marker of inflammation, but the more studies that are coming out really are showing that your mental health, your... The state of inflammation, your... Even things like epilepsy. Epilepsy and cancer are tightly linked to the level of systemic inflammation measured by... Just with one biomarker, hs-CRP.

So, optimizing our nutrition to eliminate processed sugars and reduce overall glycemic load will pay big dividends when it comes to reducing systemic inflammation, neuroinflammation. And I think something needs to be said about total calories. So, any diet you follow, if you reduce the calories and create a calorie deficit, even... I hate to say this, but even in a processed food diet that's primarily processed food, but just reducing total calories, and you could do this through time-restricted feeding and intermittent fasting, is going to produce some favorable changes. But the changes will be exponentially better if you improve the quality of your diet, so instead of just the quantity. It's important to create a calorie deficit, but the easiest way to create a calorie deficit is to improve the quality of what you're eating, it becomes astronomic, because it's not overtly triggering neural circuitry that's making you want to eat, and its re-establishing metabolic flexibility and metabolic control much easier. So, optimizing our nutrition, measuring these biomarkers, and really focusing on what I like to call just biometric biomarkers or functional biomarkers. If you can do X amount of push-ups and chin-ups or whatever, and I saw your push-up challenge with Gabrielle, so... And that was impressive. If you can do that...

SHAWN STEVENSON: I'm not doing it with you. You've been under water for 10 days. And you exercised under water too, didn't you?

DR. DOMINIC D'AGOSTINO: Well, yeah, we did. That was part of what we had to do. Yeah, yeah.

SHAWN STEVENSON: Of course, you did. Of course, you did, Dom.

DR. DOMINIC D'AGOSTINO: But just improving upon our function through excise, primarily resistance training, instead of aerobic training, resistance training will pay the biggest

dividends because you're building skeletal muscle mass, which increases not only skeletal muscle mass, but bone density. And that it's that skeletal muscle mass which is the glucose sink. So our metabolic health is tightly coupled to the amount of muscle we have and us using that muscle. And I think that's going to reduce inflammation tremendously, just having more control... Metabolic reserve, if you say.

SHAWN STEVENSON: Awesome. I'm so glad that you tied that together. We've talked about... Go ahead.

DR. DOMINIC D'AGOSTINO: Yeah. And that was a little bit over-simplistic, but I think we're still kind of... We don't fully understand what is triggering neuroinflammation because there are some people doing everything right. There are some people who have nailed their nutrition, some people who've optimized our diets, and some people who look like physical specimens, but they still have neuroinflammation. So, in this case, I think it's important to look at the potential for a pathogenic pathological agent, pathogenic agent causing this. So, this could be a bacteria, it could be a chronic virus, so...

SHAWN STEVENSON: Could be a toxicant.

DR. DOMINIC D'AGOSTINO: It could be a toxicant. So that was the next thing. But I would urge people to, especially if they're in the Northeast or anywhere, really, to get tested for Lyme disease or to look at Epstein-Barr virus or CMV or herpes simplex virus, or if you're older, to get a shingles... To get tested for shingles, and that... 'cause some people... And then maybe it seems to be more prevalent post-COVID, and I don't want to kind of get into whole... That discussion. But it seems like our immune systems are sort of hyper-activated now in a way that is triggering or increasing the pathogenicity of these chronic microbes that we may have. So that's an area of research that we're very interested in because there's some compelling data to.

To basically link some of these viruses to Alzheimer's disease, so viruses can cause chronic neuroinflammation, herpes simplex virus, Epstein-Barr, there's quite a bit of research on that and potentially Lymes disease too. So, it's a very... I was going to say nascent field, but people have been studying this for some time, and there's good data accumulating that points to various infectious agents as being triggers for neuroinflammation, and I would then go back to that, once you've dialed everything in and you're optimizing as much as you can, but you still have sort of chronic headaches or neuroinflammation or these episodes, you might want to look at various infectious agents causing that.

SHAWN STEVENSON: No, this is still pointing us to a place of empowerment. What can tend to happen, even with the outcomes coming from viruses, which there are some data even, COVID

finding its way into the brain, is that there's nothing we can do about this. And even when you started off the conversation with Alzheimer's disease, again, knocking on the door of being in the top five causes of death in United States, right now, six or seven, and less than... I mean, if you put together some of the best data on this, less than 5% of this is due to true genetic defects a lot of this has to do with our environment, our lifestyle and the like, has a huge influence. The same thing holds true with the expression of infectious diseases and viruses and the like, why are we seeing this happen right now at this degree? We are as a society, we're the sickest nation truly in the history of recorded... It's chronic diseases specifically, in recorded human history. Our epidemics of obesity and insulin resistance and cancer and heart disease, the list goes on and on, it's creating a state where we're far more susceptible to these things, so it's the opposite of resilience. So, our bodies being able to manage... Because as you've mentioned these viruses, the majority of people carry some form of a herpes virus, for example.

DR. DOMINIC D'AGOSTINO: Oh yeah, mm-hmm.

SHAWN STEVENSON: And it can manifest due to these stress inputs and the stress... Now, when you're stacking conditions against you with stressors, be it from your diet, emotional stress, environmental stressors, that's when these things can kind of take hold. What if we stack conditions in our favor in the opposite direction? That's what your work is really about, and I'm glad that you brought this up with the exercise component. And you've been testing environments, we're talking about extreme environments to see what humans can actually do, and we can take on some of these things in our day-to-day life. So, I want to ask you about this, and I know this is going to... This is a tough question. Alright, but this is one of those things that people tend to want to know is, what are some specific things that we can eat that can support our resilience? And I'm going to throw one out here. Researchers at Auburn, so we're talking about neuroinflammation, they uncovered that Oleocanthal-rich extra-virgin olive oil was effective at helping to reduce neuroinflammation, specifically helping to heal the blood-brain barrier.

DR. DOMINIC D'AGOSTINO: Oh yeah.

SHAWN STEVENSON: I didn't have a dog in the fight, I didn't care if olive oil was remarkable. I got it like... I do have a bias because it's been utilized for so long and it's such a low processing method to make it, but the data, when I saw that, I just like, "There's something really special about this."

DR. DOMINIC D'AGOSTINO: So, olive oil for the record is my favorite fat, so extra-virgin olive oil. It's rich, you get a good quality extra-virgin olive oil, and it has, it's rich in polyphenols, it has a little bit a bitter and even kind of a maybe, describe it as a hot taste. I have no less than...

Always a quarter cup, so of olive oil... A quarter to a half a cup of olive oil, I think, a day, of rich... And that's a lot of calories. You work out the calories and it's a lot, almost like a 1000 calories of olive oil. I'll make dressings with it as the base, and I also put MCT, so it will be like an MCT, olive oil dressing, so you're getting ketogenic fats on top of the olive oil. Yeah, there're many foods that we just shouldn't necessarily... And this is an issue with the ketogenic diet, was that the ketogenic diet, the classical Ketogenic diet was a 4 to 1 ratio in grams of fat, four parts fat to one part combination of protein and carbohydrate. So, four parts fat, if you work out the math, the percentage is something like 85% to 90% fat, is a classical ketogenic diet. So used for epilepsy. An issue with that is that no consideration was really taken to consider what types of fats were part of the diet.

So, it was mostly saturated fat, dairy fat, and even hydrogenated fats back in the day, and it still worked, even with all that, but we have so much room for improvement in the types of fats that we're incorporating into our ketogenic, and aside from ketogen, let's just talk about low carb, because a ketogenic diet is really a medical therapy, it's rather extreme. Let's just talk about a low-carb diet, which is... Maybe you call that a modified ketogenic diet, a 1 to 1 ratio of fats to proteins and carbs. So extra-virgin olive oil, monounsaturated fats should be the predominant fat in your diet. I'm not hyper-critical of saturated fat, but if you can bring that down to 20% or less. The early ketogenic diets were almost all saturated fat, but if we bring that down and make the cornerstone of the fat within our diet monounsaturated fats and olive oil being a large percentage of that, that's going to be super important. So Oleic acid, so eggs surprisingly have very little saturated fats and they're super rich in phospholipids and choline in vitamins, and so egg yolks are like... Eggs and fish and grass-fed meats, but even if you can't have grass-fed, just beef is fine.

We tend to eat organ meats. We eat a lot of heart, and we eat a lot of liver and I eat a lot of small fish, like sardines and have a lot of mackerel, so that's what I had this morning, mackerel. And nuts, I use to some extent, but not a whole lot. If I eat a lot of nuts, I think I just tend not settle too well, but yeah. So, the cornerstone of the fat composition in a low-carb diet, ketogenic diet, should be monounsaturated fats and also a...

A higher percentage of omega-3 fatty acids. And when you look at the omega-6 to omega-3 ratio, you really want that to be... The modern diets are something like, I read, 20 to 50 parts omega-6 to omega-3, it's highly, highly skewed towards these omega-6, pro-inflammatory fats, where you should kind of... Some authors talk about five to one, but when I did the math on my diet, it's more like three to one, some days almost one to one, so if you could do a three to one omega-6 to omega-3 ratio, I think that's great. I mean, if you could do a one-to-one ratio of those fats, so docosahexaenoic acid, like DHA and EPA are super important for biological membranes, our immune system, our... They're basically taking a low-dose NSAID drug, but they have many benefits on top of that.

And so, yeah, so when you talk about specific foods, fish and eggs should be top of the list and organ meats should be thrown in there, beef and chicken. I kind of prefer Turkey. We eat wild game a lot at our house, but with fish, you have so many different kinds of fish too. So, you can do shrimp, you can do oysters and muscles and things like that, and there's just... You're getting things like selenium, which are super important, not only for detoxification, but for antioxidant enzyme systems, things like that. So, you're getting a lot of micronutrients that you would otherwise not get if you're just eating chicken and broccoli or whatever. So, I'm a huge fan of broccoli too, but yeah, and then let's talk about carbohydrates, what you can and can't have. I'm a huge fan of... When I think of carbohydrates, I just think of fiber, so fat, protein, and fiber. So, the protein can come from the sources that I was just talking about. Green, leafy vegetables, the more green and darker, the better, and you're going to get that chlorophyll, you're going to get micro-nutrients. And salads are salads that are rich in colors, broccoli.

I'm a huge fan of broccoli and broccoli sprouts. Chlorella and Spirulina are two supplements that I often take when I'm traveling, and I don't have access to eating salads or things like that. When I lived in the undersea environment, one of the things, because I knew I was in a high oxidative stress environment, the partial pressure of oxygen was higher and things like that, I couldn't have salads or fresh vegetables, so I was taking ENERGYbits, which is a Spirulina and Chlorella supplement, but it's highly, very dense in that, and it's rich. And you're talking about a food that's functioning as a very powerful antioxidant supplement, and it's also a form of protein. So, when we go to space exploration, we have to build bio-regenerative systems to grow these vegetables that are going to be super important. Broccoli will be super important things to incorporate into the diet, in addition to protein sources that need to be engineered and figured out too.

SHAWN STEVENSON: Awesome. What's so interesting about Spirulina, for example, is that NASA actually kind of pressed it back into popular culture. This was in the 1980s, when they were initiating research that it could be a nutrient-dense source of nutrition for astronauts. Right?

DR. DOMINIC D'AGOSTINO: Absolutely, yeah, yeah.

SHAWN STEVENSON: And the crazy thing is, of course, it's been utilized for thousands of years as a protein source from cultures in different parts of the world, whether it's South America or Africa, and to have it be like a potential space food really speaks volumes about the nutrient density.

DR. DOMINIC D'AGOSTINO: It does, yeah. So yeah, not only is it a source of protein, but it's a source of, can be a source of omega-3s and it has a super-rich array of antioxidant compounds

that can offset the oxidative stress environments, and that's why I took Spirulina, ENERGYbits supplements in that, and I would... Ideally, we want to be able to grow our own in space. The former Director of NASA Life Sciences, Dr. Marshall Porterfield is actually spearheading a huge project in regenerative farming at Purdue and creating a big bio-dome facility where a lot of these regenerative technologies are going to be employed to basically design, engineer and optimize the life support and food systems in space. So yeah, he's a good trend of mine and really spearheading this whole regenerative ag thing. That's going to have profound implications in space, but like many technologies that are developed by Department of Defense and NASA, or DARPA, like GPS, which got me here, are, the public is going to use. So, the public is going to benefit tremendously from this kind of research in regenerative ag. And I'm excited because I grew up on a farm, and we live on a farm. I'm a neuroscientist, but I'm a kind of a farmer deep at heart, so I'm super interested in, yeah, these agricultural technologies.

SHAWN STEVENSON: This is one of the things that really stands out about you that I admire is the fact that, again, you being somebody who's living on a farm and putting yourself into these extreme environments as well, whether it's under water, whether it's knocking on the door of being in space and putting these things to the test, but also educating and sharing what you learn. Right now, you shared you got two continuous glucose monitors on.

DR. DOMINIC D'AGOSTINO: I do. I got an Abbott Libre and a Dexcom G6 on the other end. So, I'm comparing the two, as far as accuracy and precision, and also reliability, 'cause I bang around outside and do a lot of physical work outside, and sometimes other ones are more prone to be knocked off than the other, so vetting it out is important.

SHAWN STEVENSON: Both of us are big fans of Levels as well.

DR. DOMINIC D'AGOSTINO: Oh yeah.

SHAWN STEVENSON: And they've got such a great... The reason that I love them, one of the reasons is their data points in their collection, and being able to kind of stratify that for us to take those little pieces, like what are some of the most likely kind of culprit foods out there? And things of the like. And also, by the way, guys, Levels just opened up because they were in beta for a long time, they just open it up where you can get access now, and they've got a new version of it where you don't have to check in with your phone. I don't know if you know about this.

DR. DOMINIC D'AGOSTINO: Yeah, yeah.

SHAWN STEVENSON: Of course, you know. Of course, you know. Anyways, go to the levels.link/model. That's L-E-V-E-L-S dot link/model. The waiting line is over, you can get access right now. I just got a new one at home, and then seeing you, you're doubled up...

DR. DOMINIC D'AGOSTINO: I'm doubled up.

SHAWN STEVENSON: So now I'm like, I'm definitely going to go today or tomorrow and put on the new one and give it a trial run. I learned so much just getting that feedback even from different time today, stress levels, all the things, of course we attribute it towards our dietary intake, but it can provide us with a wealth of information you can have right there in your hand. It's personalized for you.

DR. DOMINIC D'AGOSTINO: Absolutely. Yeah. And that's why I partnered with Levels. There's a lot of CGM companies out there, but they were... And I've talked with all of them prior to being an advisor for Levels, that they were super interested in improving the existing technology, so through research. So, they were going to put money behind research and determine and do as much research as possible to optimize their product as a tool for metabolic optimization. And we are specifically using continuous glucose monitors and the Levels app as a behavioral tool to influence the behavior around eating choices to optimize your diet, and this is a non-diabetic. We have a registered clinical trial looking at non-diabetics, and I think that's where this really comes into play.

And I even know insurance companies are really putting money into this idea that if you have a whole family history of... And everyone over 50 has type 2 diabetes, then people within that family at the age of 30, 40 or whatever, should have a continuous glucose monitor to preemptively monitor postprandial glycemic excursions, if you want to make it scientific, and glucose fluctuations in response to meals. And so that individual can make better choices on the types of foods they're eating, on the amount of food that they're eating, and they could... Insurance companies can pay a lot of money later or they can pay a little bit of money now and actually reimburse patients who may be predisposed to diabetes. So, I think this is a super important thing.

But people, they don't have to wait for their insurance company to cover it. This technology is available through Levels, and most importantly, a CGM just gives you your glycemic variability throughout the day. What the Levels app does is it gives you highly actionable information and tells you what to do, and you get a metabolic score that is part of a complex algorithm that looks at the rate of rise, area under the curve, complexity analysis of the CGM trace and all these things, that will give you actionable information about what you should eat and you shouldn't eat, and even exercise and sleep. All this data is sort of incorporated into the app, and it's been very insightful for me. I consider myself a pretty insightful person when it comes

to choosing, but there were some foods that I thought... I knew I didn't quite feel well after I've eaten them, and the CGM really elucidates and clarifies why that's the case.

SHAWN STEVENSON: It's fascinating, especially again, coming from somebody like you getting that stamp of approval on that is remarkable. Again, it's levels.link/model. And man, it's so awesome talking with you, and I just really appreciate the work that you're doing and the way that you're going about it, because it's important. Like, right now we have an opportunity to help shift culture, so you're involved in so many different areas of that. And if you could, could you let people know where they can follow you? Where they can get more information, just get into your world.

DR. DOMINIC D'AGOSTINO: Well, thanks for asking. Yeah, so I really appreciate what you're doing in the podcast world and bringing your expertise and information to a huge audience, which we have... Our lab was super motivated for educational outreach, as you have been, and we created the Metabolic Health Summit. So, I'm a co-organizer for that. And that was in Santa Barbara a few months ago. Rhonda Patrick was one of our keynote speakers, as was John Rowe, who got me into this whole field. So, I would encourage people to go to Metabolic Health Summit, we offer CME credits, and you could do that, and there's a lot of content that's still there that you can get educational credit for, and I think that content will be available until October. So, everybody in the space, so many people that... Many of your listeners are familiar with were speakers at this event.

So Metabolic Health Summit, please check that out and the content that's available, 'cause we had a whole virtual platform. And my website is ketonutrition.org Ketonutrition, all one word, dot O-R-G, and we have a blog every two weeks on different subjects. The last one was on lean mass hyper-responders, why people get elevated LDL cholesterol on a low carb ketogenic diet, which is a question I get asked most, so check out that blog. And we also have a newsletter, so please sign up for our newsletter at ketonutrition.org. And I send you things in advance, sort of the cutting-edge products that I'm using, I'm testing, and different science or podcast that I'm doing. So, this podcast will go into our newsletter and sent out to all our subscribers, and I'm excited for that to come out and share this information.

SHAWN STEVENSON: Awesome. The blog is amazing. The articles you share there are so good, and I wouldn't expect anything less from you, man. And again, thank you just for being who you are. Thank you for stopping by to share your wisdom, I appreciate it.

DR. DOMINIC D'AGOSTINO: Thanks for having me, Shawn, appreciate it.

SHAWN STEVENSON: Thank you so very much for tuning into the show today, I hope you got a lot of value out of this. Such an important tool to have in our superhero utility belt is the

awareness of this ketogenic framework. And what we're talking about really, again, is just changing the information that we're utilizing for cellular communication, and what we're making ourselves out of the energy substrates. All of those things can tend to get compartmentalized in science today, but they all work together in one sovereign human being. All right? So how can we stack conditions in our favor? Let's keep this tool for when we need it. There are also, of course, performance applications. There are applications with cancer as one of his primary fields of research. There are applications with weight loss.

But this doesn't mean that it has to be the end all be-all with a ketogenic framework, it's a tool that we have access to. And to have the science behind it and to have this available to us is something really special. So again, we really scratched the surface on this topic. Dom and I had multiple conversations about some of the other offshoots of what he's working on, and things that are coming up in the future. And it's really special because we've got some really great minds out here asking these questions, testing things, and helping to see results for our citizens. But most importantly, it's about exposure and getting this education into more people's hands. It's why it's so important to continue to share the show and to be a walking representation of what's possible. That's what The Model Health Show is all about.

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