Episode 534: Dr. David Perlmutter on the Surprising New Science of Uric Acid to Reduce Disease Risk
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Katie: Hello, and welcome to the "Wellness Mama" podcast. I'm Katie from wellnessmama.com and wellnesse.com. That's wellness with an E on the end. And this episode, we went deep on a topic that was somewhat new to me, at least in the really specific data. And I'm here with Dr. David Perlmutter, who is a board-certified neurologist. He's a five-time "New York Times" best-selling author. And he sits on the board of directors and is a fellow of the American College of Nutrition. He is highly decorated, to say the least. His books have been published in 32 languages, and I have learned so much from his work. In this episode, we go deep on the science of uric acid and a lot of the data in his new book, which is called, "Drop Acid". And he talks about what uric acid is and how it works in the body, the sources of uric acid in the diet, but he goes deep on the topic of how this affects so much more than just gout, including metabolic dysfunction, which is a big issue in today's world.
He talks about why 88% of American adults have at least one component of metabolic syndrome, and how uric acid actually affects all five components of metabolic syndrome. He talks about why uric acid levels being what they are is actually a survival mechanism in humans, but how we aren't really designed for the way modern society sets up diet, and it causes this increase in uric acid. He explains how reducing uric acid levels has a positive rollover effect into all these other areas, including all those parts of metabolic syndrome, like weight gain, high blood sugar, high blood pressure, etc. He also talks about some very specific ways you can reduce uric acid in the body very, very quickly, how even in a couple of weeks, people will start to see dramatic changes in this. So like I said, I learned a whole lot in this episode. I understood what uric acid was before, but he makes it really clear to understand and gives you some tangible tools to actually start changing these levels in the body. Very fascinating episode. I know that you will learn a lot. I certainly did. So without further ado, let's join Dr. Perlmutter. Dr. Perlmutter, welcome.

Dr. Perlmutter: Katie, great to see you. Thanks for having me.

Katie: Oh, it's always such a pleasure. And I'm exited to go deep on an entirely new topic with you today. But before we jump into that, I have a note in my shownotes that you originally wanted to be a meteorologist specialising in hurricane tracking. And, living in a hurricane-prone area, I just would love to hear a little bit more about that and then what kind of changed your trajectory.

Dr. Perlmutter: "Trajectory" interesting word there. Well, I grew up in Coral Gables, which was back then the home of the National Hurricane Center. And I used to go there, it was on the campus of the University of Miami, I used to go there when I was, you know, fifth grade, sixth grade, and sneak into the building and walk around. And it wasn't just being a hurricane tracker and a meteorologist, I wanted to be the guy in the plane who went into the eye of the hurricane drop zones and measured pressures and did all the...I mean I just thought that would be really great.

And I have to tell you, interestingly, I kept that dream for a while until I got into high school and I realized that, to become a meteorologist, you had to study these really hard things like physics and calculus. And I thought I could never do that. You know, turns out, of course, for medical school we did a lot of physics, calculus, biochemistry, the whole bit. But I think I underplayed my hand a little bit. But I've always kept a real interest in tracking hurricanes. Of course, as you do, I live in South Florida as well. You live in Florida?

Katie: Yeah. Well, that's cool, I didn't know that about you. And I'm certainly grateful that you ended up where you are now because I've learned so much from you. But on that note, I know you have been doing a deep dive into a topic that is new to me and I would guess is somewhat new to a lot of listeners or at least something we've only maybe heard of in passing but never really thought about if it could be relevant to us or not. You've got a whole new book about this topic. I think, to start really broad, we're gonna talk about uric
acid but I think for a lot of us we may need a definition before we even jump into details. So, can you explain what it is?

Dr. Perlmutter: I will. So, uric acid, U-R-I-C acid is the end product of what our bodies produce when we metabolize fructose sugar, for example, alcohol, and something called purines. Purines are the breakdown product, when we eat food, of the DNA and the RNA contained in the foods that we eat. That's it, that's the only places that uric acid comes from.

Now, we've all heard of uric acid likely and that would be in the context of something called gout. Gout is, you know, this disease where people get these crystals in their big toe and it's really really painful. And it was actually very common in the early 20th century and the 19th century as well. You know, you see these graphics of men mostly suffering from gout, their toes are swollen, and they're generally overweight. And so, it should tell you that maybe there's a diet component to this elevation of the uric acid that causes gout.

Well, interestingly, now we know because of really some fabulous research, over the past two decades, that elevation of uric acid is an incredibly more important issue than just because it might give you gout, that's 4% of the American population. Turns out that uric acid is a central...here's the title of a study, "Uric Acid in Metabolic Syndrome, From an Innocent Bystander to a Central Player," that was published in 2016, meaning that we've always seen elevation of uric acid in diabetes, high blood pressure, overweight, and obesity, we always thought, "Well, isn't that interesting that these people then would have a risk for gout?" But it turns out that it's a causal event, it's orchestrating the elevation of our blood sugar, the elevation of our blood pressure, the increase in our body fat, it's playing a mechanistic role.

And that is, you know, certainly a revelation because, again, this is not your grandfather's elevated uric acid causing gout anymore, this is a big big issue because these metabolic problems are the underpin for what the World Health Organization characterizes as the number one cause of death on our planet. And those are the chronic degenerative conditions, the type-2 diabetes, the coronary artery disease, some forms of cancer, and yes, even Alzheimer's. That's the number one reason that people today are dying not from a virus. So, you know, it's the big net, it really is a big net. The exciting thing about uric acid is we can bring it down very quickly on the front end to keep it from being manufactured and, even in its excretion, bring it down, and finally give people a new tool in their tool chest to really gain control over their metabolism.

I mean metabolic issues are breathtaking. I just traveled yesterday, I got home from a trip to give a lecture on this topic, oddly enough, and I haven't been traveling that much over the past couple years and I was just astounded at what I saw in the airport in terms of, you know, you can look at somebody and pretty well determine where they are metabolically. We know that 88% of American adults has at least one component of the metabolic syndrome. That tells us that only one in eight American adults is metabolically sound, metabolically in the game. And now that we know this story about uric acid, and I think even more interesting is the history of how this was a good thing for us, this kept us alive in years gone by during our paleolithic ancestry and even, you know, our primate ancestors had this superpower, they would have elevated fructose
in their diet that would make more uric acid and that would lay down an extra layer of body fat so that they might survive during times of food scarcity. They might have a little bit more glucose in their bloodstream because of the uric acid being elevated, and that would power their brains and could help them avoid being eaten by other animals and help them find food.

But now, in the context of our modern lives when we are pounding our bodies with fructose and turning on uric acid, this is a survival signal gone astray. And that's really a central player, as these authors describe, in the most pervasive problems of our day that are not really genetic, they're related to the lifestyle choices that we make and, very importantly, we can change.

Katie: And that's astounding to me. I've heard it before but, every time I hear that stat about 88% of Americans have at least one of these components of metabolic syndrome, can you walk us through what some of those components are? Just I feel like this is a really important topic to address, and then we'll go deeper on the uric acid.

Dr. Perlmutter: By definition, yeah, metabolic syndrome is characterized you have metabolic syndrome if you have three of the following five. Elevated blood sugar. Insulin resistance. Elevated body-mass index. What we call dyslipidemia problem with your blood lipids, your good and bad cholesterol. Elevated triglycerides. And the last one is elevated blood pressure.

So, all of these are kind of the common things that your healthcare provider will be following. And having the full metabolic syndrome, having three of the five is seen in 50% of people age 65 and above. That's my age group, as a matter of fact. So, you know, by and large, these are things that we can control. And now we have a new toolbox, we can control our uric acid and rein these guys in because, you know, as I mentioned, the downstream manifestations of having elevated blood sugar or having elevated blood pressure, for one thing, totally threatening the brain. You know, in America now 6 million people diagnosed with Alzheimer's, that's a situation for which we have no pharmaceutical treatment whatsoever.

So, we've really got to focus on the idea of prevention. And certainly exercise, keeping blood sugar under control, maybe using a continuous glucose monitor, and keeping your uric acid reined in, knowing what it is and then doing things to bring it down to a normal level, or optimal level, if, in fact, it is elevated. These are things we can do right now.

Katie: And I feel like, the last couple of years, there's been more and more information coming out about how those same things raise your risk of complications from pretty much every disease, as well as your risk of the big ones like heart disease and cancer, like you mentioned, and also brain issues. And you mentioned there's a causal link between uric acid and these metabolic issues. Is the reverse true as well, that by lowering uric acid you lower these metabolic issues across the board?
Dr. Perlmutter: And that happens extremely quickly. Research that is being carried out, you know, that looks to answer your question and it demonstrates that you can lower blood pressure immediately by targeting uric acid. In other words, in a matter of weeks that people can have reduced risk for metabolic syndrome.

So, this thing happens really quickly when you suddenly shut off the faucet, when you stop screaming at your body to prepare for winter. That's what uric acid is doing, it's saying, "Look, get ready for winter because you may not have food and water and, therefore, we've gotta raise your blood pressure so that we can still send blood to your organs and we've gotta have a reserve of fuel so that you can stay alive."

And interestingly, when we burn fat as a fuel, we create two things, we create carbon dioxide and we create water. So, storing body fat is a resource for water when we might otherwise become dehydrated. That's an incredibly powerful survival mechanism for our ancestors. Right? But nowadays there's really no reason that we need to be packing on the pounds. There's no advantage to that, only a disadvantage.

Katie: Gotcha. And okay, there's several directions I wanna go from here but can you talk a little bit about your case and the role that mutations play in this? Because there's gonna also be some personalization and individualization within this as well, right?

Dr. Perlmutter: That's right. It's a really interesting story, and that is...so, having high blood sugar, insulin resistance, making excess body fat, those are great things. Those are really really good things if you lived in paleolithic times, you didn't know where you'd get food. Or even before that, you know, even in our primate ancestors, especially, germane to our discussion, during the middle Miocene period...and for those of you who aren't so familiar, that's like, 14 to 18 million years ago, the world became cooler. Over about a million years, this presented a bit of a challenge, an environmental challenge for survival. Right? And the people..."the people," the primate ancestors that would have survived were those that had a superpower. What was the superpower? They made a little bit more fat. I'm not saying they got obese and were walking around, you know, being very heavy but they had just a little bit more body fat. And that allowed them to survive and then pass on whatever it was in their DNA that gave them the superpower.

And what we've determined, a really interesting review and "The Scientific American" talked about this, what we've determined is that those changes in their DNA, and there were several of them, were in the genes that made what you brought up, this uricase enzyme. "Uricase," based on the name, “ase” from uric acid. It's an enzyme that breaks down uric acid. We developed mutations in that uricase gene such that we didn't make it anymore. We don't do that anymore, we don't make uricase, we don't break down uric acid. That was our superpower. Because our uric acid levels would raise, more body fat, higher levels of blood sugar, raise our blood pressure, hence survival. And here we are having a conversation.
So, that was passed on to all of us, to all human beings, to every human being alive today walking the earth. We all have the mutations in uricase. And it explains why humans have uric acid levels that are four to five times higher than the uric acid levels of other mammals.

So, we are predisposed to having a high uric acid level because, for the almost entirety of our time on this planet, that was a good thing. That allowed us to survive basically in the times of food scarcity, especially fructose. You know, we might get some berries in the late summer, early fall and that would powerfully signal us that winter was coming. It would change our gut bacteria. It would signal us to immediately make body fat. And importantly, what uric acid does is it damages mitochondrial function, which is something we sure as heck don't need today, but the advantage of that is it would slow down our metabolism so we wouldn't burn fuel as readily.

So, you know, interestingly, when we see, for example, a bear that's getting ready to hibernate, they are just smoking, as relates to making and storing body fat, and their metabolisms are ratcheted down so they're keeping that energy store so that they can then hibernate and then burn their body fat. So, unless, you know, any of your viewers are planning to go into a cave for 4 or 5 months and hibernate, we don't need this extra resource of calories because calories are far more than abundant today. But it's not just calories, it's really specifically fructose. Our fructose consumption has increased between 1970 and 1990 a thousand percent. And that fructose is tapping into this ancient signaling pathway telling our bodies right now, "Prepare for winter," 365 days a year. And the winter doesn't come. So, we're laying down body fat creating a calorie resource. We really don't need to be doing that, look at the downsides.

Our life expectancy is declining. And that decline began pre-COVID. Yes, it declined quite dramatically with COVID but it began pre-COVID. And it's really not that we suddenly developed a genetic change but it's because of this evolutionary environmental mismatch that we are, in our environment, confronting our evolution, confronting our genome, confronting our physiology with signals that it is ill-equipped to respond to.

And interestingly, in the book, you probably read this, I wrote my first paper, published my first paper on this topic in 1971, which was 51 years ago, when I was 16. And I concluded that paper by asking the question, you know, "What about us? We're living with this outdated machinery. We have machinery that's geared for our ancestors, stemming from our genome. And now we're challenging it day in and day out with these influences like fructose and telling our bodies," you know, "to do things." And the body responds. It's doing its best based on the signals that we give it in terms of the foods, for example, that we eat.

Katie: That statistic about we're seeing life expectancy decline is actually the reason I got into health as well, reading, when my first child was a baby, that his generation was gonna be the first in centuries to have a shorter life expectancy than their parents. And like you mentioned, we're still seeing this trend continue, which was really alarming for me.
And I highly recommend the book for all of you guys listening. It is a fascinating read. And I know that there's so much more information in there than we can go into today. But when you talk about how excess uric acid is reducing mitochondrial function and leading to metabolic dysfunction, that, obviously, leads to the question of, "How do we undo this damage when we're living in a society where all of this is very abundant?"

Because it seems almost like a magic lever, when you read this book, of, "Oh wait, this is a thing that can help with weight loss. It can help with metabolic dysfunction. It can help reduce disease risk. It becomes a big deal." So, where do we start?

Dr. Perlmutter: It does become a big deal. And I'll answer that question in just a moment but, you know, the question many of your viewers may be thinking, I'm thinking right now, is, "Why would I, as a neurologist, be involved in metabolic issues?" And, you know, for me, as a neurologist, understanding that metabolic dysfunction is at the core of our most pervasive neurodegenerative conditions, that's what motivated me and now we recognize that, you know, it's at the cornerstone of heart disease and kidney disease and non-alcoholic fatty liver disease. These are all manifestations of a dysfunctional metabolism. So, it does indeed throw a wide net.

So, to answer your question we need to do everything we can to, first, understand what's going on, what uric acid is doing, that it was a survival mechanism for our ancestors but now it is killing us, and then get a sense as to where we are on the scale of our uric acid level. And then, if it's high, we'll talk about in a moment what we can do.

So, first of all, how do you know your uric acid level? Well, the simplest thing to do is call your doctor and say, "By the way, with my blood work that was done last month, 6 months ago, last year, what was my uric acid?" And be prepared for the response being, "Well, you don't need to worry about it. You don't have gout." Right? You'll hear that. Or the next answer that I also like, I don't know if I really like it, is, "Don't worry about it, it's in the normal range." And important because, you know, we're smart enough to know numbers, A and B, "normal range" is not so great. We want optimal. You know, "normal" these days, that's not our goal to be what normal or average is. So, they'll tell you that, "You're below seven milligrams per deciliter, so, you're fine."

And as it relates to gout, that's a reasonable number, if that's your only focus in wanting to know about your uric acid level. Because it's above seven that you're at increased risk for gout and it's above seven in the blood that uric acid begins to precipitate out and form crystals. So, that's a valid number only in the context of gout. As it relates to cardiometabolic issues, we want our levels to be around 5.5 or lower. So again, call your doctor's office, say, "BTW, what was my uric acid level last year?" or go in to the doctor or call the doctor and say, "can you call the lab? I want to stop by and get a uric acid level done."
Or nowadays, which is so exciting, you can get your uric acid level done at home. You can do it yourself with a little monitor that is much like...here's what it looks like. And that's my most recent level. And this is like you did your blood sugar in the day, you put a small tiny drop of blood on a stick that goes in the machine, and the next thing you know you know your uric acid level. So, these are non-prescription, they're available online, anybody can buy one. Once you know the level then you can begin to understand how your diet and other lifestyle choices are affecting it. It's like measuring your blood sugar, knowing which foods are gonna spike your blood sugar, whether you're doing your fasting glucose or using a continuous glucose monitor.

So, knowing uric acid is right there with fasting blood sugar, with blood pressure, with body-mass index. A powerful player, as it relates to metabolic health. And I know this is new material for a lot of people. Not for everybody, there are some forward-thinking healthcare practitioners who've been dialed into this for a few years, but I am really excited that we're really really early in the game in terms of understanding uric acid. And I think, more importantly, just how threatening to our health fructose really is.

Katie: And I feel like people are familiar with fructose, hopefully. But I also think maybe a lot of people don't realize some of the dietary sources of this. Like we often think, "Okay, fruit. Got it, that makes sense," but this is far beyond just fruit. And arguably, like you said, some fruit at certain times of the year could actually be beneficial or would be within normal human consumption. But can you walk us through maybe some of the other foods and maybe like timing? Is there time of the year when it's better or worse to consume more or less fructose?

Dr. Perlmutter: Well, first, let me say that fruit is certainly a good thing to eat. And we don't wanna go hog wild, you know, an apple a day keeps the doctor away but five apples a day and the doctor you will pay. But the beauty of the fructose in fruit is at least three-fold. Number one, it's not a real high level, we're talking 4 or 5 grams of fructose maybe in an apple.

Number two, the speed at which we consume and expose our digestive system to fructose is really important. You don't really expose your body to a high fructose load when you eat apple or eat a fruit as you would, for example, if you drank a soda. So, the speed is slowed because you're eating it, number one, but also because you're consuming fiber and fiber is slowing your absorption as well. That's really a good thing. Fruit contains vitamin C, which is on our list of the right things to do because vitamin C helps us excrete uric acid. And finally, there are various polyphenols, bioflavonoids in fruits and vegetables that do contain some fructose, I might add, that directly target an enzyme that our bodies use to make uric acid. And they're very effective in terms of reducing uric-acid creation.

So, fruits and vegetables are on the table. Again, not over the top on consuming a lot of fruit. And, you know, there are certain fruits that are really high in fructose, like mango, which is unfortunate because I have a big mango tree in the driveway, but, you know, other things like tart cherry are certainly on the table. Reasonable
tart cherry is especially on our list because tart cherry contains in it certain things that help reduce uric-acid production. As a matter of fact, if you look at the cover of the book, there on the “O”, that's a cherry. And that's exactly why we put it there.

So, it's important though to recognize that fructose is in probably 60% of packaged foods at the grocery store. Think about that. So, it works its way into our diets when we don't even know it. But I think it's really fundamental that the amount of fructose and its delivery is key. That is, if you're drinking 36 grams of sugar in your coke or other beverage that you're drinking, that is an onslaught to your body that quickly overrides your intestinal ability to deal with fructose and immediately sends that fructose to the liver where the party begins and the damage is done and your body is preparing for winter.

Now, surprisingly, that also happens with fruit juice. And what am I saying? I'm saying that fruit juice is a powerful resource for fructose and there's nothing natural about it. It's not as if our hunter-gatherer forebears would suddenly come upon a forest where there were trees with cartons of orange juice or apple juice hanging from the trees. So, that bombardment of your body with that level of fructose is really telling your body, "Get ready for winter, make as much fat as you possibly can very quickly." So, those are important sources of fructose.

Alcohol is an interesting story as well because a modest consumption of alcohol is either neutral in men or actually is associated with slightly reduced uric acid levels in women. Again, the bioflavonoids contained in alcohol may be effective in that regard. Hard liquor will raise uric acid, but the biggest player is beer. Beer has alcohol but it also contains our third category, which are called the purines, as mentioned, the breakdown product of the cells of whatever you're eating, specifically the DNA and the RNA that is contained in those cells. Beer is made from brewer's yeast and that's really a powerful source of purines. So, now you have the alcohol, you have the purines, we understand the beer belly. Right? It's because you're sending two powerful signals to make uric acid, you know, harvesting this pathway, telling your body to make fat. So, that's what the biochemistry of the beer belly really is.

So, it's important then to limit how we, you know, consume those resources to make uric acid. And I do wanna mention one other thing and that is our bodies, as an emergency signaling mechanism, will make fructose within our body. So, you can be fructose-free but if you have, for example, eaten a lot of salt, your body thinks it's dehydrated. And one of the things it does is activates, what's called, the polyol pathway and makes more fructose. Fructose is a hedge against dehydration. Why? Because fructose becomes uric acid and uric acid makes body fat.

Well, how does body fat have anything to do with dehydration? Simple. When we have more body fat and we're using that for our metabolism, we're making carbon dioxide and water. So, we make water from fat. So, this whole pathway has another very important effect on us for survivability and that is that it allows us to have water.
When you look at this animal that walks across the desert for 3 weeks and doesn't drink water, it's carrying a resource for water on its back called "the hump of the camel." And inside that hump is not water, it's fat. And it's stored outside of the camel so that it doesn't insulate it so that it can deal with the heat. But believe me, it taps into that fat for calories, that's for sure, but also as a water resource. And many animals do it. That's why whales have a lot of fat. Even the hummingbird, 40% of its total body weight is fat as it's preparing for this epic multi-thousand mile journey that it takes. And if you want a hummingbird in your backyard, what do you put out there? What's the hummingbird food? It's sugar water. They love that. And that's what allowed them to survive.

Katie: That's fascinating. And I'd love to understand the salt connection a little bit more, especially related to dietary salt and degree of consumption. Because I know salt is also a part of culinary experience and people use salt quite often. Do other minerals come into play here in a balancing way at all, like magnesium or other minerals?

Dr. Perlmutter: We are really kind of exquisitely sensing, as a survival mechanism, our sodium level so that, when sodium levels go up, we trick our bodies into thinking it's dehydrated. At which point mechanisms are activated that help us conserve our body water, as it were, activation of something called vasopressin, a brain hormone. And that vasopressin, intriguingly, in and of itself also, triggers fat production. That's new information. I mean we always had vasopressin acting in the kidney to help us conserve water, as a survival mechanism, that's for sure. But we sense the elevation of sodium.

The bottom line is we have sensors that actually sense what's called osmolarity, how many particles are in our bodies. And the other important particle that will increase our osmolarity is glucose. So, having a high blood sugar, you know, this is America where 83 million people are pre-diabetic, 36 million people are diabetic, type-2 diabetic, and that's, you know, close to 40% of adults having higher blood sugars, signaling their bodies to make more fructose, that signals their body to make more fat and to raise the blood sugar even further. So, it becomes a feed forward pathway to make us more and more insulin-resistant and fatter. As a survival mechanism, that's what it's supposed to do and trying to help us, but in the face of the foods that we are eating, we are sending the wrong signals.

It's really well and good to deconstruct our foods and look at them in terms of the fat calories, carb calories, protein calories, the micronutrients, macronutrients. Great. You know, I live and breathe that stuff. But the reality is we should take a step back and look upon our foods as information. Foods inform our physiology as to what to do. Foods are changing our microbiome milieu, and that has implications in terms of our metabolism. When our consumption of sodium goes up, our bodies think it's dehydrated and, subsequently, make more fat. And that can be, you know, sitting in front of the TV and eating a bag of salted pretzels. That sends a signal to your body that winter is coming because you're making more fructose immediately, activating that pathway.
Now, a simple offset for that, and I don’t recommend it, I don’t recommend the pretzels nor do I recommend the fact that they’re salted, I mean that’s a very, you know, highly processed carb as it were, blood sugar is going to go up, that drives fructose formation even more rapidly in conjunction with the sodium. But if you happen to do that because you’re watching a big game, or whatever, and you know it was wrong, drink a lot of water. That'll help keep the blood sodium lower and won't trigger this pathway.

And let's be clear, this pathway leading to the production of uric acid, which then damages mitochondria, has been demonstrated to be in the human brain as well. The activation of this polyol pathway to convert glucose into fructose into uric acid to then damage the mitochondria...and, you know, that's a central player in Alzheimer's, in Parkinson's, really across the board in neurodegenerative conditions.

Katie: You just said so many important things. And I'd love to touch on the water one a little bit because I've noticed a trend in the health community, often people who lose weight and resolve metabolic dysfunction, one of the things they talk about as a pillar of that is they weren't drinking enough water and now they're trying to consciously drink enough water every day. And we can all think of like Captain Planet and dilution as the solution to the pollution but it seems like proper hydration is a big key in a lot of these different elements.

Dr. Perlmutter: That's right, you know, eight glasses a day, whatever it was, you know. And a lecture I gave...was it yesterday? Yeah, it was the day before yesterday. And I said to the audience, "Yeah, you're gonna be peeing a little bit more. You are. And there's nothing wrong with that, that's a good thing, keeping your system able to eliminate waste products. All good." But what you said is really true, that we're just not drinking enough water. And a powerful tool to help us with this signaling pathway is to dilute down our sodium consumption by drinking more water. So, you're 100% right.

Katie: And then you also mentioned that these are all things that are built in survival mechanisms and those are actually a good thing. I feel like often we are kind of consciously trying to fight our body into doing something we want it to do but we're not working with the built-in mechanism of our body to do that. So, how do we turn this on its head? Like what are some of the ways we can signal our body, "Hey, it's summer. We don't need to gain weight. We need to lose weight," and like how do we reverse that trend? What are some of maybe the optimal guidelines?

Dr. Perlmutter: You kind of hinted at that earlier about seasonality. And, you know, the real thing about seasonality, as it would relate, for example, to eating the berries and the fructose-containing foods in the late summer and early fall, would have been to prepare our bodies for food scarcity. So, we don't need to be seasonal in that regard. Is there an upside to having some berries? Sure, there're great polyphenols, fiber. Good things in berries, that's for sure. But I think the notion of being seasonal...there's nothing else about our life that is seasonal, that's for sure. We experience warm weather, we experience cold weather. You know, and we I think are able to adapt to that acutely but the notion of preparing for winter by laying down extra body fat I think is an interesting throwback to, you know, times gone by. We don't need to do that now. We
are not going to be in food scarcity mode during the winter months, that's for sure, so there's no need for it. We don't need to raise our blood sugar to power our brains, our blood sugars are gonna be just fine.

In a lot of people, as mentioned earlier, blood sugar is already elevated. That's 40% of American adults. So, we don't need to trigger that pathway. We don't need to raise the blood pressure to make sure that our organs get enough blood supply. We know that, you know, high blood pressure is already an issue in the 12 to 18-year-old group. Ten percent in America of 12 to 18 year olds are suffering from hypertension. So, you know, we don't need to do that either. All of those things, the elevation of blood pressure, blood sugar, body fat, you name it are powerful threats to our physiology, our health, and certainly our longevity.

Katie: So, you mentioned that these are things that can reverse relatively quickly, like we can start to see these levels drop relatively quickly. What does that look like, especially maybe for someone who is in that higher range, either at risk for gout or at risk for metabolic issues, how quickly can they turn that around? And maybe what are some of those really important first steps?

Dr. Perlmutter: Within a couple of weeks. There's 1 study out out of England that looked at a group of 22 young men with elevated blood pressure and elevated uric acid. And they were given a nutritional supplement called Quercetin. Who knew, right? And this 500 milligrams of Quercetin in, I think it was over an 8-week period, dropped their uric acid levels by 8%. Which is pretty astounding. So, I'm just gonna make sure I got that right. Yeah, it was an 8% reduction, 500 milligrams.

And we know that Quercetin targets an enzyme called xanthine oxidase. I don't mean to be too technical but that's the target of the gout drug called Allopurinol. So, this is a way of targeting the exact same chemical pathways that the drugs work to lower uric acid. So, interesting, that's just adding in some quercetin. Who knew? There's another one that's also really effective called Luteolin and does the same thing on par with the drug Allopurinol. In other words, working just about like the drug.

So, let me go through just some nutritional supplements. We've talked about diet. And these nutritional supplements can either target uric-acid production, help with its excretion, or look at some of the other factors that this whole pathway is known to amplify. Quercetin would be 500 milligrams a day. And call me back to Quercetin later on because there's a few other things I wanna mention about it. Luteolin, another health food store bioflavonoid, that would be 100 milligrams per day. The next would be about 1,000 milligrams of DHA, yes, the omega-3 DHA.

Now, DHA is not going to have any direct effect on uric acid per se but DHA dramatically offsets some of the downsides of fructose consumption as it relates to the liver. And we could have another podcast on DHA with respect to the other things it does and why I find it so valuable for the brain. And vitamin C to help with excretion of uric acid, 500 milligrams per day. And the final would be chlorella, chlorella vulgaris. And that
would be a dosage of 1,200 milligrams per day. The reason that chlorella is on the list is because we've got decades of research that have demonstrated how effective chlorella is in terms of the issue of non-alcoholic fatty liver disease. That is an immediate consequence of high levels of fructose consumption made worse by elevated uric acid. So, we didn't this time want to, you know, give people a list of 12 or 15 different supplements that they should be taking, because people probably already are, but really try to tease out those that are gonna have particular relevance as it relates to uric acid.

Katie: And I know, from at least the research I'm seeing, non-alcoholic fatty liver disease is on the rise quite drastically currently. I would guess most people have at least heard that term, but for people who aren't familiar, can you just give us a brief description of what that is and what's going on?

Dr. Perlmutter: Sure. So, we've known that alcohol consumption, we've known this for an awful long time, leads to damage of the liver. And the first thing that occurs in the liver is it starts to accumulate fat. Something about alcohol flips a switch within the liver that says, "Make fat." Ultimately, that fat within the liver leads to inflammation and, ultimately, this can lead to actual scarring of the liver called cirrhosis and, ultimately, liver failure. And this early on begins to compromise the way the liver can do its job.

The liver is an incredibly fascinating organ in terms of the multitude of things that it does. We've gotta do everything we can to take care of the liver. That might be actually my next book. I don't know, the more I learn about liver function, the more excited I become about it. So, that's alcoholic fatty liver disease. Well, it turns out that fructose consumption can cause the exact same changes within the liver, the flipping on of the fat switch, turning on fat production, making those liver cells retain fat, ultimately compromising function, and downstream issues like insulin resistance, increased triglycerides, dyslipidemia, increasing blood glucose, etc. So, fructose can do the same thing. And that is called non-alcoholic fatty liver disease.

Let me get a little technical here because this is kind of exciting for people like me. And hopefully, I can break it down and tell you why I'm interested in this. Turns out that, if you block the metabolism of fructose by dampening down or breeding laboratory mice that don't have a particular enzyme called fructokinase, that's the first enzyme in the metabolism of fructose. If you do that and give these animals alcohol, lots and lots of alcohol, they don't get fatty liver disease. What is that telling us? It's telling us that the way that alcohol is causing damage to the liver goes through the fructose pathway. And what we now understand is that alcohol consumption, the way we know that alcohol consumption increases uric acid formation too, but we know that alcohol consumption activates the pathway we talked about earlier, the polyol pathway, whereby your body makes fructose internally, endogenously. Alcohol turns that on. But if we can block the metabolism of fructose, at least in a laboratory animal experiment, we don't see that they get fatty liver disease. So, interestingly, this notion of alcoholic versus non-alcoholic fatty liver disease seems to have the same mechanism, which is, again, mediated by fructose.
Katie: That's so fascinating. And I love getting to put all these pieces together and how often there's overlap between things that are helpful for this are also helpful for the brain or for the heart. It's like how amazing, the body completely works together.

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But you mentioned, to circle back on Quercetin, am I pronouncing that right, hopefully, but I wanted to hear a little bit more about that because you said to remind you about that.

Dr. Perlmutter: Sure. So Quercetin is a nutritional supplement, it is a bioflavonoid. It's a health food store item and I mentioned how incredibly effective it is in terms of reducing uric-acid formation in the human body, certainly in laboratory animals, that's for sure, but in the human body as well. And that's one of the reasons it's obviously on our list. Quercetin does a lot of other things, it's an anti-inflammatory, it's an antioxidant in
and of itself. It is a senolytic, meaning that it helps our bodies get rid of senescent immune cells and allows us to repopulate with more vital youthful immune cells, therefore helping us have a more balanced immune system. These days, who wouldn't want that?

And the other thing that's really interesting about Quercetin, I'm gonna be technical again, so, here it comes, this will be on the quiz though, it activates a pathway called the AMPK pathway. The AMP kinase pathway. And simply stated, that is a pathway that says, "Don't make fat. Burn a lot of fat," and instructs your liver not to make more sugar, glucose specifically. It turns off when you stimulate AMP kinase, AMPK. There are a lot of YouTube videos that people can watch on this. If you stimulate AMP kinase, it shuts down a process called gluconeogenesis, forming glucose, new glucose in the body, "genesis," creating it.

And interestingly, probably the most popular drug for diabetes is called Metformin. And that's what Metformin does, it stimulates this pathway, AMP kinase, that, again, tells your body the hunting is good, no need to store nuts away for the winter, right, "Don't make body fat, don't raise the blood pressure, don't raise the blood sugar. Everything is good, the hunting is good, we've got plenty of food."

Now, uric acid works in the opposite way, it shuts down AMPK. As you would expect. It's doing its job, it's saying, "Winter's coming, we don't have food. Make fat, raise blood sugar, increase blood pressure." So, that's powerfully then why we want to get our uric acid levels under control.

I will mention that probably the most effective thing that we can do to stimulate AMPK, you know, including Quercetin, but it's exercise. Exercise is the ticket that allows us to activate AMPK. And, you know, that's why we see so many benefits from exercise, along with, you know, obviously, other things that it does.

Katie: And you also mentioned, in the book, the LUV diet. Can you explain what that is and why it's important?

Dr. Perlmutter: You gotta love it, right? So, the LUV diet is LUV, and that means lower uric value. So, we created a really nice explanation in terms of what your food should look like. And the nice thing about the LUV diet is it's a diet that's going to work with probably almost any other diet that you may be on. So, you can be on the LUV diet if you are paleo, keto, vegan, whatever because we've just put in these important bullet points that target uric-acid formation regardless of the diet that, you know, a person might think this is what they've chosen to do.

And basically, it is a diet that, as you would expect, is low as can be in terms of anything with added fructose or added sugar, for that matter. Remember, sucrose or table sugar is 50/50, fructose bonded to glucose. So, even using table sugar you're pounding your body to the tune of, in America, 58 pounds a year of sugar. So, it's a diet then that is very restrictive as it relates to sugar. It's very high in various foods that are known to
contain the various bioflavonoids. I've been talking about that help with lowering uric acid. We talk about the one beverage that helps lower uric acid called coffee. And it can even be decaf coffee, it may well be the caffeic acid or other polyphenols in coffee that are helpful. Which I was really very happy to find out, being a coffee drinker.

And so, we've created these 40 recipes that feature many of our hero foods like onions, like the cruciferous vegetables, cherries, for example, that target specifically uric acid and allow you to eat really really well. And, you know, this notion of lowering your uric acid might be, for many of your viewers, that one missing link that they kept thinking, "I'm doing all the right stuff," you know, "I'm exercising each day, I'm careful what I eat but I'm just not getting that final piece of the puzzle here. I know there's something else I could be doing."

And now what we're seeing is, when you target uric acid, I'm not gonna say "the icing on the cake," you know, we're talking about sugar, but, you know, it may be that missing link that people have been knowing that it's out there for a long time, they just didn't know what it was.

Katie: I was definitely blown away, when I read, at how clearly you break it down. And it seems like almost a miracle idea of how many things in the body this seems to affect. And especially when we're talking about weight loss and metabolic dysfunction, these are things that people can very often feel very stuck in. And so, I feel like it gives a very tangible measurable thing that people can focus on that has really positive rollover in every other area. So, I thought that was very hopeful and extremely timely in today's world.

Are there any other lifestyle factors that come into play here? I know, in general, you've written about this in your other works, sleep is a super important component. Does it have any direct effect with uric acid? You mentioned exercise and hydration being big, any other lifestyle factors to pay attention to?

Dr. Perlmutter: I'll get there. And if I don't, you'll call me back. But one thing I just wanted to mention, we didn't really mention it, we talked about alcohol, we certainly have talked a lot about fructose, the third component, which are the purines. And there are certain foods that are definitely associated with raising uric acid because they deliver a lot of purines. And I'm not gonna say they are completely off the table but something to think about, if you've done the other two and yet your uric acid remains elevated, you would begin to limit your animal-based purines. And these are organ foods, organ meats like liver and kidney, and certain seafoods like shellfish, scallops and mussels, certainly game like venison as well.

And I know there are upsides, for example, the liver with the iron, the B12, for sure. I never eat liver because I never liked liver. Never could I eat liver from age 5, or whenever it was that my mother was making liver, I'll never forget it. But that said, I know that perhaps some of your viewers eat those organ meats, and I'm gonna say with good reason, there are some good nutrients there. But let's see what your uric acid levels are doing. So again, the fundamental here is to know your uric acid level and then you realize how much work you need
to do or not. So, you may get away with having that liver that you so desire because you know it's good for you or you like it or whatever.

But that said, there are other lifestyle factors that we should consider and talk about. And it is true that people who don't sleep well have a higher uric acid level. And interestingly, what we know is that, for example, people who have sleep apnea become briefly hypoxic. You know, when you do a sleep study on these people, you put a pulse oximeter on their finger and you see that their blood ox saturation levels go down. People are familiar with that term now because it's something, you know, in terms of COVID, that they've heard about. So, the amount of oxygen in the blood goes down, that's a powerful signal to turn on the pathway to make fructose from glucose and then make uric acid. So, that might well explain why people with disruptive sleep, people who aren't sleeping enough or having restorative sleep seem to have a higher uric acid level as well.

So, getting a good night's sleep, and that means two parameters, how long you're sleeping and what is the quality of sleep, in my opinion, would be the reason to use a wearable device to track how well you're sleeping. I wear, what's called, an Oura Ring. It's very helpful for me to understand how long I've slept and what is the quality of my sleep.

Exercise, in general, is a good thing to keep uric acid level low. But I wanna just let your viewers know that, if you one day really go way beyond your normal bounds of exercise, normally you run 3 miles a day and now you've run 12 miles a day, you can expect for the next day or so that uric acid level is going to be elevated because you're breaking down your own muscle tissue and, as such, you're liberating purines into your system that are going to help raise uric acid. As a matter of fact, the purine story would reveal that, as it relates to forming uric acid in your body, two-thirds of your purines are coming from your own tissue breakdown and only a third, generally, in most people, unless they're eating huge amounts of meat, only a third is coming from the diet. So, that's I think very important.

And as long as we're on that topic, I will say that fasting or going deeply keto for a couple days is going to transiently raise uric acid. The good news is that it's one step backwards but two steps forward. When it's said and done, that uric acid level is certainly where it was before or perhaps even a little bit lower.

So, the point is that, you know, there's a good reason to fast, amongst the many many other reasons that certainly you've talked about and people have talked about for a long time, but I think that, you know, we're now hearing about the notion of time restricted eating. And we actually dedicated a section in the book to talking about time restricted eating, meaning the notion of compressing the time in the day that you eat instead of eating, you know, all the time that you're awake, you have your breakfast at 7:00, you end up, you know, having dinner at 7:00 or 8:00 at night, that you shorten that window to maybe 8 hours or 10 hours. Meaning that you have then a built-in fast that you don't eat anything after dinner and that you have your break fast or the first food of the day at 10:00 in the morning or noon or, in my case, it's often 1:00 or 2:00 in the afternoon so that you're having every day a period where your body is not getting food. Which does some remarkable things for your physiology, helps offset a lot of the metabolic issues that are related to elevated
uric acid. And the other thing it does is it never ceases, in my case, to make me grateful that, once it's time to eat, that I have food to eat. So, it does amp up that gratitude center in your brain. And I think that can't be anything but good.

Katie: That's good to know about fasting. That was gonna be one of my questions because I've certainly seen benefits from fasting and it's good to know that, even though it may have a short-term effect of raising uric acid, long-term it's still a net positive. And there may not be a lot of research on this yet but it makes me so curious because you mentioned the seasonality and light is also such an important signaling mechanism for seasonal changes and also just 24-hour circadian biology. I'm curious, is there any component of getting natural light and it coming into play here? I know you've talked about it in relation to the brain and in other ways but is there any connection specific to uric acid that we know of from light?

Dr. Perlmutter: I would say that anything in the body that's going to increase inflammation, and we know that when we're not aligned with circadian rhythm, as Satchin Panda has made so evident to us, that we are at risk for metabolic issues, we are at risk for weight gain, we're at risk for increased inflammation and increased production of stress hormones, etc.

Now, all of those things are certainly, you know, seen with elevated uric acid. And my sense is they're certainly going to amplify uric acid. And I can tell you that, when we see anything, for example, that is associated, like being dyssynchronous or not honoring our circadian rhythm, that these things are associated with increased risk of diabetes, certainly insulin resistance, that moves us to the formation of more and more fructose in the body. Remember, higher levels of glucose become higher levels of fructose. What happens to the fructose? It becomes uric acid.

So, this is really very straightforward and easy to understand that, when we are working the night shift or that we are not getting to sleep on time because we're exposed to blue light or really allowing our bodies to experience full spectrum light in the morning, for example, and that melatonin levels aren't doing what they should do and, therefore, there are downstream consequences from that, which are metabolic, these are going to amplify the uric acid signaling pathway.

Katie: It makes sense. And I feel like I could talk to you all day because you're such a wealth of knowledge, but I also wanna honor your time. So, briefly, before we wrap up, where can people find the book? Because there's so much more in there that was amazing information that we didn't have time to cover today. So, if people wanna keep going and learning, where do they find it?

Dr. Perlmutter: Sure. It's everywhere.. it's everywhere you wanna be. No, but "Drop Acid" is on all the online booksellers, at local bookstores, it's at the airport bookstores, it's really everywhere. If you wanna learn more about it, the website is dropacidbook.com. So, it's pretty straightforward.
I do a lot of YouTube videos about the topic now that are really instructive. I include keynote slides, and people seem to be liking those. But again, the book would be on any of the online retailers. It's reached number one now on Amazon, in nervous system diseases. So, very excited about that.

Katie: And I'll include those links as well for all of you guys listening. Those will be at wellnessmama.fm. And a couple last very brief questions, the first being, if there is a book or a number of books besides your own which have influenced many other lives but ones that have deeply influenced your life, what they are and why?

Dr. Perlmutter: Well, I think I'm gonna give a very nerdy answer to this question. I mean I think I would guess many of your guests would talk about a book that really moved them spiritually. And that, you know, certainly has happened to me. But I think the most exciting book that I have is, believe it or not, my medical school textbook of biochemistry by Stryer. I don't know if you can see it behind me but it's that book right there. And it's always nearby, it's very very close. And right next to it is Adams and Victor's Principles of Neurology. I mean I know that sounds nerdy, you were probably looking for "Siddhartha" by Hermann Hesse about...and I get that, you know. But in terms of just...I mean I'm understanding biochemistry now like I never did before.

And it's absolutely a revelation that, yeah, you know, we had to learn the pathways, this becomes that, how is glucose metabolized, sure, get it, but now I'm beginning to understand why these things are happening from a perspective of our health and physiology today. But, more importantly, and certainly, as you can see, more excitedly about how they evolved to be protective of us and allow our survival. So, reading through and re-studying the biochemistry, it's really pretty exciting for me. And again, I get that's probably not an answer that anyone would've expected or have been looking for.

Katie: Well, I'm appreciative for that answer and appreciative for you doing all that deep dive research and then converting that into easy-to-understand information in your own books that we can all implement easily in our own daily lives. And lastly, any partying advice for the listeners today that could be related to this or something entirely unrelated?

Dr. Perlmutter: Yeah, I would say that we live in a world where we are kind of...not kind of, clearly being messaged that we should live our lives come what may, do whatever the heck we want, and, when we have a problem, that modern medical science is going to be there to take care of that problem. And that's really unfortunate because it's just not true. I mean, you know, you see people who have high blood sugar and are taking their diabetes pills. You see people taking so-called Alzheimer's drugs that don't even work for that matter. So, I think the message would be that we have to be our own stewards of our health destiny. And we can be when we are empowered by knowledge. To learn what we can be doing day in and day out to keep ourselves healthy, that is I think a very very important message that people can grab onto.
We have tools. We know the right things to do. I mean you've been talking about this information for an awful long time, it just takes doing it. And again, don't feel that, you know, it's okay to fall back and let your doctor handle it, they're not the arbiters of your health destiny. You are.

Katie: I think that's a perfect place to wrap up. And you give some very actionable information related to that in the book, definitely, highly recommend it for all of you listening. Very fun read and so much information. Dr. Perlmutter, I'm so grateful for your time today. It's always such a pleasure talking to you.

Dr. Perlmutter: Katie, great to see you again. The last time we saw each other I think was in Austin, wasn't it?

Katie: It was, yeah.

Dr. Perlmutter: Right? At the after-dinner thing, after the event at the dinner, I think, that, you know, we took a bus to. Anyway, great to see you again.

Katie: You as well. Thank you so much for your time.

Dr. Perlmutter: You bet.

Katie: And thanks, as always, to all of you for listening and sharing your most valuable resources, your time, your energy, and your attention with us today. We're both so grateful that you did. And I hope that you will join me again on the next episode of "The Wellness Mama Podcast."

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