Nitric Oxide Basics and What Depletes It

So again, if you're using mouthwash, you have to stop. Switch from a fluoride-free toothpaste or fluoride toothpaste to fluoride-free toothpaste. Stop using antacids.

Find a way to work with your physician to wean off of them, whether it's over-the-counter prescriptions. And then use continuous glucose monitors. Anything that causes an increase in blood sugar, don't do that again.

Because glucose is glue, as the name implies. It sticks to things. It sticks to enzymes and proteins and renders them dysfunctional. So if you do those four things, no fluoride, no mouthwash, no N acids, and no sugar in your diet, then you've released the brakes on the body's ability to naturally produce.

Welcome, everyone, to the Longevity Leaders podcast. I'm your host, Dr. Rudy Mueller, and today we have a special guest that I'm very excited to interview, Dr.

Nathan Bryan. Now, Dr. Bryan, I have been in your classrooms at seminars for years, from A4M to IFM to, you know, integrative in the Congress for Integrated Medicine out of New York City.

That's right. I have seen you and utilized your products for a while. So it's such a pleasure to be able to actually have you here. Thanks for following me.

It's been a journey and it's great to be with you. So I would think that, I don't know, father, the grandfather of nitric oxide, I've been doing it a long time.

You have been. So if you could, just give us a little bit of background on yourself, where your research, where you started out with research, coming across nitric oxide as being an important molecule for the body, and then where we're kind of headed today.

Sure. Well, you know, I'm a small town Texas boy, went to school at University of Texas, got a degree in biochemistry, then quickly realized the job market for a bachelor's degree in biochemistry wasn't great.

I enrolled at LSU School of Medicine. I completed a PhD in molecular and cellular physiology. And it was at that time, this is the late 90s, early 2000s, and a Nobel Prize had just been awarded for the discovery of nitric oxide.

So it was an interesting time, it was an exciting time in physiology and biochemistry. And so that's really what started my interest in nitric oxide. I was training under a pharmacologist.

Dr. Bryanu2019s Research Journey and Discovery of Nitric Oxide

I met Lou Ignaro, one of the guys who shared the Nobel Prize, and I finished my PhD on really developing analytical methods where we could detect really low levels of nitric oxide in biological tissues.

And then from there, I did a fellowship at Boston University Medical Center, really trying to still understand nitric oxide in vascular biology. And then from there, I was recruited for my first faculty position at the University of Texas Health Science Center in Houston by Fred Murad, one of the other guys who shared the no-go prize.

And so Dr. Murad was my department chair for a number of years. And that really started our research because I was at what's called the Institute of Molecular Medicine.

And we were charged specifically to understand the mechanism of the disease to the extent that you could develop rational therapies. And so we started figuring out, number one, how the body makes nitric oxide, number two, what

leads to a natural loss of its production.

And then once we understood that, then and only then could you start to develop rational product technology. Or drug therapy, which is where we're at now.

Right. And so with nitric oxide and that whole process, what particular conditions were you seeing, okay, the nitric oxide is something that we are depleting or is a depletion of nitric oxide that may be contributing or even foremost causal or primary to this symptom sign generating?

Is there a particular thing that really jumped out at you early on? Well, early on, the data came from in animal studies, so we could knock out the enzymes that makes nitric oxide and then look at the symptoms or the phenotypes that develop from that.

So in a moment, if these animal models were deficient in nitric oxide, the enzyme that produces nitric oxide, they develop instant resistance, diabetes, high blood pressure.

They seem to not perform as well cognitively in terms of maze and memory recall. So that told us that nitric oxide was more than just a vasodilator, right?

It was an incredibly important signaling molecule that controlled a number of things from insulin signaling and metabolic disease and cognition, high blood pressure, erectile dysfunction, exercise, and tolerance.

So those are the key observations, and then even later on, we and others discovered that there's oral bacterium that are responsible for maintaining optimal nitric oxide production.

So then we started to interrogate, okay, what about all these antiseptics? What about overuse of antibiotics? What about fluoride in our toothpaste, which kills the microbiome?

So today, we understand that anything that destroys the oral microbiome, or any microbiome for that matter, causes systemic disease. And we can partly explain that through the inhibition of nitric oxide production.

Yeah. So early on, when first hearing about nitric oxide before hearing your lectures, it was L-citrulline, L-arginine were trying to utilize to boost nitric oxide levels.

There was no great test to look at nitric oxide available to the clinician that's in practice every day. So, but now, I mean, you have just hit on some amazing things here when it comes to, well, why does nitric oxide become depleted?

Or to what are some of those contributing factors in the oral microbiome being one of the major ones? And so we realized very soon after hearing your conversation or a lecture, well, L-citrulline and L-arginine Yeah, those companies don't understand the basic biochemistry.

Exactly, yeah. And so there are other things that we can be doing to help support this. And not just from, hey, take this supplement to increase your nitric oxide levels, but what is that root cause upstream driving factor?

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Yes, so today we look at what's disrupting the enzymatic production of nitric oxide from the nitric oxide synthase enzyme and what's destroying the oral microbiome.

And if we can maintain normal enzymatic function and we can maintain a healthy microbiome, not just in the mouth, but in the gut, on the skin, everywhere, then we can optimize human performance.

And so if we give the body what it needs, remove from the body what it doesn't need, the body heals itself. And medicine and science has made it way too complicated.

How Oral Microbiome Health Affects Nitric Oxide

But no, so that's what we're focusing on now is, and we certainly understand the enzymology and the biochemistry. How do we restore and maintain optimal enzymatic function?

And then how do we maintain an optimal oral microbiome? And many times it's not implementing new strategies, it's stopping the things that we know are disrupting that.

In terms of affecting the enzyme, we have to stop eating a high sugar, high carbohydrate diet. Anything that leads to an increase in blood sugar, we know completely causes endothelial dysfunction and NOS dysfunction.

And then, you know, the simple things like getting rid of fluoride in your toothpaste, getting rid of fluoride in the drinking water. If you're using mouthwash, you must stop.

And then the other big contributor to nitric oxide deficiency is RN acids, the proton pump inhibitors, the omeprazole, pentopra, the protonics, Prevacid.

You know, these are now over-the-counter medications, and they're very dangerous. Yeah, meant to be taken for seven to 10 days. People take for seven to 10 years, right?

15, 20. Oh, I know. And now the clinical data show us that people have been on these drugs for three years or longer have about a 30% to 40% increase in heart attack, stroke, and Alzheimer's.

It's not increased risk, it's increased events. And then mechanistically, we know that's happening because it's completely shutting down nitric oxide production.

And so how does the body convert nitrates, nitrites into nitric oxide? Well, in the 1970s, it was the first discovery that when we consume nitrate-rich vegetables, that the kidneys reabsorb about 25% of that.

And then they intentionally concentrated in our salivary glands. And in the 1970s, we didn't know why the body would intentionally do this. But today we understand that there's nitrate-reducing bacteria that live on the crypts of the tongue.

And by the way, nitrate is inerting humans. If you don't have the right bacteria and you eat nitrate-rich meals or take nitrate capsules, which many companies are selling, you just excrete it out in your sweat, your urine, and your feces.

So in order for diet to provide a nitric oxide benefit, we must have the right oral microbiome. Because these bacteria are converting nitrate into nitrite, and this is a two-electron reduction.

And again, with two out of three Americans using mouthwash, 99 out of 100 people using fluoride toothpaste, 73% of the municipalities in the US putting fluoride in their drinking water, the majority of the people don't have the right oral microbiome.

So they're not getting the nitric oxide cardioprotective benefits of their diet. And if they're taking things like beets or beet capsules or nitrate capsules, they're not getting a clinical benefit from it.

And then the other thing is if you don't have sufficient stomach acid production, you don't get the benefits of it. And there's over 200 million prescriptions written for antacids every year.

200 million prescriptions written for antibiotics every year. And now two out of three Americans are using over-the-counter antacids. So the point here is that everything we're doing is inhibiting nitric oxide production.

What are the results? Two out of three Americans have an unsafe elevation in blood pressure. Nine out of 10 Americans are unfit, metabolically unfit. 50% of the men over the age of 40 report erectile dysfunction.

I mean, we're a mess. And we've provided an explanation that partly explains why Americans are so unhealthy. Yeah, and it's a lot of the removal of these things from our everyday life to be able to address it.

And so when you're testing, if you're looking at nitric oxide levels, I remember these strips. Is that a valid way to? You know, I developed those strips back in 2010. So I filed patents.

I was still, in fact, with the University of Texas at the time. And in about 2012, I abandoned the patents. The University abandoned those patents because, number one, it's old chemistry.

It's called the grease reaction. What we're doing is looking at a diazo compound form from nitride and a sulfanilamide that turns pink upon it. So what we're measuring is salivary nitrite.

So they're not nitric oxide test strips. as they're advertised. We're not detecting nitric oxide, because nitric oxide's a gas, right? But what we thought at the time was it gives us an indication of the presence or absence of these oral nitrate-reducing bacteria.

But the challenge we ran into, and the reason I abandoned the patents, and the reason I don't use the test strips anymore, is because if you've got an active oral infection, we're going to pick up a local immune response in the oral cavity, and it's going to turn that test strip bright pink.

But yet people present clinically with symptoms of nitric oxide deficiency. They may turn this test strip pink, but they've got ED, they've got high blood pressure, they're diabetic.

And so it gives them a false sense of security because systemically they're nitric oxide depleted, but in their saliva, because of an active oral infection, they light up the test strip.

So, you know, it's still a good tool, I think, because there are no false negatives. If you test negative and you don't turn colors on the test strip, then it tells us you're nitric oxide deficient.

But it doesn't tell us why. Is it because you like the bacteria? Is it because you're taking an antacid? Is it because you're using mouthwash or fluoride or you have endothelial dysfunction?

I mean, I know how to do that. I can interrogate that and get the answers to it. But now these companies that are out there selling these test strips, they don't understand what they're actually measuring.

Okay, that's good to know. Is there any test that we can look at and even if we have to infer as a secondary test to look at nitric oxide levels or is it just based off of signs and symptoms and it's pretty straightforward that we might be having?

Well, there are some really important functional medical devices that look at what's called flow-mediated dilatation.

Testing Nitric Oxide and Functional Vascular Measures

And so there's a number of these FDA-cleared medical devices on the market, but what it's looking at is how responsive your blood vessels are to certain agonists like shear stress or brief periods of ischemia.

So I always recommend those because those are functional tests. They're not biochemical too. The endoped is one example. There's others, and that's called ischemic pletmisography, so we occlude the blood flow and the brachial artery for five minutes, we release the cuff, and then we look at the degree of vasodilation.

And then there's some non-aschemic plenistography looking at arterial compliance and pulse wave and augmentation index. But all of these are functional measurements on vascular health.

But what we try to preach is, pay attention to symptoms. Because if you have ED, you have nitric oxide deficiency. If your blood pressure is above 120 over 80, that's some degree of nitric oxide deficiency.

If you have insulin resistance, that's a symptom of nitric oxide deficiency. But really, I tell people there's only two people in the world who need nitric oxide.

There's the people who are sick and want to get better, and then there's people who are well and don't want to get sick. So if you fall in one of those two, then you should consider nitric oxide as a potential, not just treatment, but a prophylactic kind of daily regimen to maintain optimal nitric oxide production because honestly, The food that's grown in America is nutrient depleted.

We're exposed to toxins, EMFs, herbicides, pesticides, environmental toxicants that are almost always kind of compromising our ability to naturally produce nitric oxide.

And destroying the bacteria that help produce it. And destroying the microbiome. Very interesting. Okay, so what are the solutions for someone that is wanting to support the nitric oxide, whether they are sick and need to get well or well and want to avoid being sick?

What are the solutions and what are the strategies here to be able to raise nitric oxide? A supplement, a tablet, what's your go-to? Well, our first is always kind of diet and lifestyle, right?

Because my belief is about chemists and physiologists is if you give the body what it needs and remove from the body what it doesn't need, there's no need for supplementation.

There's no need for drug therapy. Let the body heal itself. But because of the conditions we live in, that's almost You know, it's not realistic. So again, if you're using mouthwash, you have to stop.

Switch from a fluoride-free toothpaste or fluoride toothpaste to fluoride-free toothpaste. Stop using antacids. Find a way to work with your physician to wean off of them, whether it's over-the-counter or prescription.

And then use continuous glucose monitors. Anything that causes an increase in blood sugar, don't do that again. Because glucose is glue, as the name implies.

It sticks to things. It sticks to enzymes and proteins and renders them dysfunctional. So if you do those four things, no fluoride, no mouthwash, no N acids, and no sugar in your diet, then you've released the brakes on the body's ability to naturally produce.

But we can stimulate that. We can activate it. Modern physical exercise. We used to say 20, 30 minutes of moderate intensity exercise a day is sufficient.

Now, you know, four to six minutes of high intensity interval training. You increase your heart rate. You increase your breath rate. Nasal breathing. You know, because we have this enzyme nitric oxide synthase in our upper airways and the epithelial cells.

And when we nasal breathe, it activates these enzymes and we generate nitric oxide. And if we mouth breathe? And if you mouth breathe, not only are you bypassing the sinus, but you're destroying the microbiome.

You're fully oxygenating the mouth, changing the environment, changing the ecology, and you get halitosis, you get dysbiosis, and we know the dangers of mouth breathing.

Right. And then the other is 20, 30 minutes of direct sunlight a day. And then, yeah, when all else fails, we have product technology that does it for you.

Lifestyle Strategies to Restore Nitric Oxide

Okay. So one of the things that I'm curious about when you talk about going fluoride free toothpaste, if we're trying to address the oral microbiome, what is, is there a strategy?

Is there a toothpaste that you would recommend that helps like a prebiotic or a probiotic toothpaste or? Yeah, I've been dealing with that for 20 years, so I've been using a non-fluoride toothpaste for 20 years, but when I looked at the ingredients on the ones I was using, and I tried a dozen or more of these, there were still things in there that seemed to destroy the microbiome, the biofilms.

So that's a year, well, probably two years ago, I started on this journey. How do we develop a microbiome-friendly nitric oxide activating toothpaste?

And so I launched this a couple of months ago. It's called Cario Smalls. This is great. Okay. Yeah. So it's fluoride-free, number one. It's hydroxyapatite-based, so it re-mineralizes the teeth.

But we also put components in there that are prebiotics that allow for these non-pathogenic commensal bacteria to repopulate and improve the diversity.

Because in a paper we published in 2014, we showed that the greater the diversity of the oral microbiome, so we were doing tongue scrapings and then culturing these bacteria, the better the blood pressure management.

So, how do we improve the diversity of the microbiome? How do we improve the numbers and communities of these nitrate-reducing bacteria? And that's the purpose of the CardioSmall toothpaste.

It's a prebiotic. It kills the pathogens because we're providing a source of nitric oxide while you're brushing your teeth. And most pathogenic bacteria are sensitive to nitric oxide.

It binds to the iron sulfur centers of them, shuts down the respiration, where the non-pathogenic commensal of nitric oxide producing, so they're resistant to it.

So now we've got a solution to selectively kill oral pathogens while maintaining healthy, diverse, non-pathogenic commensals. And we're modifying the salivary pH, which is a huge problem.

So you're getting a, you know, it's a two-pronged approach, killing two birds with one stone in the sense that you're, I mean, yes, you're remineralizing teeth, but the focus here is killing the bacteria that can be causing a problem and getting rid of those as well as repopulating through the…

Yeah, and creating an environment where the natural ecology of the bacteria, where the ecology can support the healthy microbiome and diverse. So no, that's a huge undertaking for us because a lot of people aren't looking for nitric oxide products, and I think that's why education and awareness is so important, but hopefully everybody brushes their teeth.

And these are once a day or hopefully twice a day. So if you can now integrate this nitric oxide focused toothpaste and just replace your existing toothpaste, what we're finding is that their blood pressure comes down.

And hypertension is the number one driver, the number one killer of men and women worldwide because if we're restoring the oral microbiome, we're enhancing nitric oxide production and we're supporting healthy blood pressure.

So that's a major step. And think about the public health impacts of that and the global policy and the impact, the economic burden on treating cardiovascular disease and diabetes, which are symptoms of nitric oxide deficiency.

Then next year, I developed a mouth rinse that basically is going to do the same thing because even though the toothpaste does a very good job of freshening your breath, improving teeth mineralization, and supporting healthy microbiome, there's still people who just want to use a mouth rinse before they go out, before they go on a date.

They just like that feel. Two out of three Americans are using mouthwash now that's killing 99.99% of the bacteria in their mouth, as the commercials tell us.

But how do we create a rinse that supports the microbiome, kills the pathogens, and leaves you with a fresh breath? So we finally cracked that code. We're doing stability studies now, but similar things.

We're finding in people who have resistant hypertension, you switch to our toothpaste, you use our mouth rinse, your blood pressure comes down. And it's a nitric oxide related phenomenon.

I mean, that's huge. That's huge.

Microbiome-Friendly Toothpaste and Mouth Rinse

I remember, you know, when we first started down this road of nitric oxide as a practitioner, yes, I mentioned L citrulline, L arginine, but then utilizing these different tablets or capsules to try to boost it, which would give you a temporary boost, but wasn't getting to the root issue.

Yes, we would have a temporary improvement maybe in our athletes and their ability to withstand an aerobic exercise because they feel better with the nitric oxide.

Yes, we have a lowering of the blood pressure temporarily. But with this, this is getting to the root issue. The motive is, it's very difficult to change habits.

It's the most difficult thing to change one's habits. But implementing these very simple strategies, the things you do on a daily basis, brush your teeth, use the mouth rinse if you will.

just simply utilizing a better form of this, now your body is going to improve its ability to make nitric oxide. And then once people see the results, it's easier to maintain these practices.

They're going to feel better, their blood pressure is better, they're going to be able to work out better, they're going to have more energy, their sex life is going to improve.

And now they've got a motivation because they're seeing the differences, they're feeling the differences, so what did I do different? I started this, I focused on nitric oxide production, and I'm reaping the benefits.

No, it's just replacing. You're not having to replace it. Right. And that's a huge thing to add to change. Just replace. Yeah. And then in the future, you know, we're developing drug therapy.

We're going to develop other products, you know, like a nitric oxide-friendly deodorant, not an antiperspirant. But, you know, people develop… odor because of bacteria, dysbiosis.

I haven't used a deodorant and antiperspirant in more than 25 years, and I don't have body odor because I'm supporting a healthy microbiome and I'm not allowing the colonization of the odor-causing bacteria.

Same thing with the gut bacteria. People who have odorous feces have dysbiosis. And so again, understanding how do we support the microbiome instead of destroying it, it leads to overall better health.

Sure, absolutely. Well, Dr. Bryan, it was an absolute pleasure when you see your book here, The Secret of Nitric Oxide, so practitioner lay person friendly.

It is. I've taken really the complex science and distilled it down into a lay version, sixth grade reading level. But the motivation of this book was twofold.

Number one, communicate the latest science on nitric oxide. Because as we touched on, there's a lot of misinformation out there on how do we restore nitric oxide production.

So in the book, I tell the story of what nitric oxide is, how it was discovered, what led to a Nobel Prize, and why everybody in the world should be concerned about their own nitric oxide production.

But then in that journey, I've told my story of discovery, of how the simple discoveries and observations we've made in the over 100 peer-reviewed publications that we've published, how that led to these discoveries to really lead to natural products that restore nitric oxide production.

And now, as we move through the FDA for drugs for heart disease, we've got a drug for Alzheimer's, and we make a topical drug for diabetic ulcers and non-healing wounds, but really it's for so people understand, how do we go from here to here?

Book, Products, and Closing Remarks

And to build trust and show the science and the pathway that led to these discoveries, to where people know that when we develop products and we put products to the test, that if your body can't make nitric oxide, we do it for you, but then we fix the reason your body can't make it.

Excellent. Excellent. Getting to the root cause. Functional medicine. And then even the naturopathic, it all begins in the gut. Right? Sure. Microbiome.

That's awesome. Well, thank you again, Dr. Brian. I appreciate all the work that you do. I look forward to seeing where your N101 products continue to develop.

Deodorant sounds great. Mike's son, who's 11, needs it back. It's those early teenage years, yeah. No, but you can get the book wherever books are sold.

Amazon, Barrington Noble, nathansbook.com will provide a link. Awesome. Thank you very much. Thank you, Rudy. Thank you for tuning into Doctor Talks. We hope today's episode has enlightened and inspired you on your path to optimal health.

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