Introduction and Summit Overview

Well hi, everybody. Welcome to the Peptide Summit. My name is Doctor Matt Cook, and I'm here with my friend Doctor Nathan Bryan. In college I studied cell and molecular biology, but he went way beyond me and got a PhD.

And as and, I've actually known him for years. We met at, Cell Surgical network meeting. And he was talking about using nitric oxide to, help overall health, vascular health and to help and stem cells and regenerative medicine.

And, I've been, using his products probably for 6 or 7 years now. And, you know, I decided to have him on the summit because we're talking about peptides.

But in a few important categories. I'm, I'm coming into some other molecules that I think are real important. Either as a support, in functional medicine or as something that may help peptides get where they need to go.

And that's something that we're going to dive into today. Doctor Ryan is probably a number one, nitric oxide person in the world that I've known and is a, a fabulous teacher.

And so we're delighted to have you on the show today. Thanks, Matt. Great to be here. So, tell us, tell us a little bit about, nitric oxide and what's happening with it.

Well, you know, we've learned so much over the past 20 or 30 years, and, you know, it's still new in the scientific literature. It's only discovered in the late 70s, early 80s.

But, now it's recognized with, I think, probably over 175,000 scientific papers in the, in the published literature. That it's one of the most important molecules produced in the human body.

It controls a number of cellular activities, controls and regulates blood flow, blood pressure, oxygen delivery, and the every single age related disease is characterized by associated with a loss of nitric oxide production.

So it's now demonstrated or revealed to be causal for most, if not all, human chronic diseases. So it's clear now that your body cannot and will not get better until you restore the production of nitric oxide.

Okay. What would be when you talk about major diseases, give me the top, top 4 or 5 that you think about that are related to nitric oxide. Well, certainly cardiovascular disease.

Hypertension the number one risk factor, but pretty vast disease is typically a loss of the production of the vasodilator nitric oxide. So when you lose the ability to produce a major vasodilator in the systemic circulation, you get stiff heart.

Or do you get high blood pressure. The other, is erectile dysfunction. That's the first sign and symptom of a nitric oxide vascular endothelial problem.

Nitric Oxide Basics and Major Disease Links

The other is type two instant resistant diabetes. There's a clear role now for nitric oxide as part of the insulin signaling pathway. And then, you know, the thing that's most fearful for most Americans is vascular dementia and Alzheimer's.

It's clear from a number of studies that, the earliest stages, whether it's mild cognitive disorder and vascular dementia that precedes Alzheimer's, is due to the lack of regulation of blood flow to certain regions of the brain.

So you don't get the good nutrients in waste product buildup and get the beta amyloid plaque deposition, hallmarks of Alzheimer's. So then that that's a good one.

So then that basically means all of the biggest, most common aging problems that we know of relate in some way to blood vessels and blood vessel health.

And if nitric oxide is low, that may be kind of a causal thing. There's a whole bunch of other things that we think about an integrative and functional medicine as, strategies and ways to, support that.

But you've you've developed some ways to actually start to replace that nitric oxide in the body. Right. Well, I'll take it a step further. You know, there's inflammation is what kills, right?

That's what causes heart attack strokes. And we know that nitric oxide inhibits inflammation. And, you know, we're hit with a number of infinite number of insults every day.

From the foods we eat to the environment we're exposed to, to our lifestyle habits. But our body responds with three finite responses it's inflammation, oxidative stress, and immune dysfunction.

And nitric oxide is what controls all three of those. So if your body loses the ability to make nitric oxide, your blood vessels become inflamed. You get a lot of stress, you get immune dysfunction, and those show up as biomarkers that you can recognize as risk factors for certain diseases.

So, you know, what I tell people is that it's really pretty simple. You have to do two things. You have to stop doing the things that disrupt nitric oxide production and start doing the things that are clinically proven to promote or activate nitric oxide production.

That's really that simple. But then if you delve deeper, you gotta figure out, okay, well, what am I doing that's inhibiting my body's ability to make nitric oxide?

The number one thing is mouthwash. You know, in the United States, there are over 200 million Americans, two thirds of the population that use mouthwash on a daily basis.

It's not coincidental that two out of three Americans have an unsafe elevation of blood pressure, putting them at risk for cardiovascular disease. Most recently, it's been demonstrated that if you use mouthwash, you lose the protective effects of exercising.

If you use mouthwash, you lose the protective effects of doctors. So these are things that people do, I think, with good intentions. But there's collateral damage and people want to go out and exercise and eat eat good food.

But if you use an mouthwash, you completely eliminate the cardioprotective benefits of. So that's number one. Number two is fluoride toothpaste. If you get rid of fluoride, it's an antiseptic.

Kills your thyroid function. And it's a neurotoxin. So get rid of paranoid. Get rid of, boy based toothpaste. And then number three is antiseptic or antacids.

You know, over 200 million prescriptions are written for proton pump inhibitors every year. That's not counting the over-the-counter purchases. We need stomach acid for our body to heal.

We need stomach acid to make nitric oxide. So if people do those simple things, which is cost savings, stop using mouthwash. Get a fluoride free toothpaste and stop using an acid.

Your body will thank you for it. And you'll notice the difference. And then to promote or activate it, we gotta get up and move. We have a moderate physical exercise.

Eat a lot of green leafy vegetables that are enriched in nitrate. And then get out and get sunlight. Sunlight. There's

certain wavelengths of light that will stimulate or activate nitric oxide production.

So again, it's really six things. Stop doing three start doing the other three. Okay. The I, I avoid the, the fluoride toothpaste like the plague. And interestingly, the, the idea from the literature is, is even for people with real bad gastritis, most people are supposed to only be put on a proton pump inhibitors for a short period of time, and then even then, that generally doesn't seem like a great idea.

A lot of times, a lot of times, we find other integrative ways to kind of help people with with those symptoms. And I, I, I echo that, that often that is the beginning of kind of a downhill slide for people and and I remember when I was in college, the doctor that I had, gastritis after some weekend, you know, or some, you know, and then I remember the doctor said, oh, just you can just take this purple pill and then you can just take it.

And then I took it for about a week, and then I thought, this is the craziest thing. And then I stopped taking it. I never had it. I basically never had really a stomach problem ever since then.

So it just it, it that that was like an indication to me of something was screwed up about how we were thinking about things. Yeah. You know, those drugs were never approved for chronic use.

They were approved for acute use for gastroesophageal reflux disease. But now you can get them over the counter and you know, you get H. Pylori overgrowth, you get, you know, gastric ulcerations, you get overgrowth of, over other bacteria.

You become more prone to foodborne pathogens, and you increase your risk of heart attack and stroke by about 30 to 40%, right. That's because that that stomach is supposed to be acidic has kind of like a nice, useful barrier that keeps problems.

And so that if we lose that acidity, then bacteria can start to live in there and then the whole nitric oxide. So then, what are the ways to start?

What Lowers Nitric Oxide and How to Restore It

And now before you go into that, you talked about three things. So unlock the how because here we are in Covid days. And so then, you know, if I, if I, if you said immune dysregulation five years ago, I was like, who is that now?

The whole world suddenly interested in immune problems. Tell me about immune dysregulation and Covid and, and, nitric oxide and how you think about that.

Sure. Well, any immune response, whether it's, you know, response to an infection or exposure to a virus or a bacterium or an immune response to heal a wound, a cut or some injury in the body, the body respond with mobilizing our immune system.

You get to activate your immune system and you mobilize those to the production of nitric oxide. And then, interestingly, our own immune cells make nitric oxide when they're activated by cytokines.

And then those immune cells generate a lot of nitric oxide at the site of an infection or inflammation to kind of close off that number one, to kill invading viruses or bacteria.

So when you're when your immune cells generate nitric oxide, it binds to the iron sulfur centers of bacteria and shuts down the respiration. And it prevents viral particle replication.

So if your body can't make nitric oxide, you can't elicit a robust immune response and you become immuno compromised. And that right there explains what we've learned in two years of coronavirus and who who's most at risk for Covid infection.

It's the elderly. It's people with high blood pressure. Previous semi diabetes, obese and smokers. The reason

they're at risk is because they're compromised to make nitric oxide.

So when they get exposed to not just coronavirus, but any respiratory virus or any bacterium for that matter, their body can elicit a robust immune response.

The virus takes home, replicates, propagates throughout the body, they get systemic disease, blood oxygen saturation decreases because there's no nitric oxide to signal oxygen release.

They go to the hospital to get ventilated. And typically that's the end of the story for for most people. But it's those of us who have good nitric oxide levels like I've been.

And we have 26 clinical trials all over the US. We have a Covid drug now. In phase three clinical trials, a nitric oxide, and I've never been sick with Covid doesn't mean that I haven't been exposed to Covid.

I'm on an airplane every week for the past two years. And I typically don't like to wear a mask and breathing in my own carbon dioxide, but I've never been sick from hope.

So that explains mechanistically everything we know about not just immune dysfunction and immunocompromised and Covid patients are patients at risk for Covid, but it explains every single infectious disease, for that matter.

Now, we're seeing in our FDA approved clinical trials for nitric oxide drug patients getting better. You take our risk patients, you start them on the therapy within 72 hours of onset of symptoms, and they don't get sick.

You keep them out of the hospital completely by the hospital. You keep people alive. What drug is that? It's a drug I developed called no virus in. But it's a drug specifically for.

It's a nitric oxide releasing lozenge. And we got an eye. And for, for Covid patients at the start of the pandemic, is that similar to the nitric oxide lozenge that I've been I use it in.

So my drug company has a so we've got a different drug company that has the license for my it's a license to the same patents, but rather than the use still to be used for dietary supplements and nutritionals, we've acquired the license for drug to the same technology, same basic nitric oxide delivery.

We just increased the potency because these patients need a little bit more nitric oxide than daily maintenance. This. It's kind of interesting because, in my in my old life, I was a I was an anesthesiologist and so, but, and and it is it kind of interesting also because then what I would do is I would meet people and then I would have like 2 or 3 minutes that I would have to make a real quick assessment.

How's it going? Do you have any asthma, diabetes, heart, lung, blood pressure, kidney, liver. And then you know, if that was all normal, the probability that you have a problem with anesthesia is like 1 in 1,000,000, right.

And then on the other side of the coin, if somebody has, damn, you know, vascular disease to any of the main arteries, to their, heart, their lungs, their brain or their peripheral blood vessels and any heart disease or metabolic syndrome.

You got to think really carefully, because that's where almost all your complications are. And, and that's because, when they go under a fairly significant physiological stress, I think one thing that's happening is almost all of those people are low in nitric oxide.

And so then and I, we didn't even understand this really. I mean, we understood it mechanistically, but we didn't have anything we could do about it, you know, from, an anesthesia perspective, but that vascular sort of metabolic syndrome, inflammatory pattern that people had, you'd walk, you'd walk in and you, you figure that we would as archeologists, you look at that and you're aware of that and about, you know, 30s, and, and and in a way that's almost like an analogy for Covid.

Covid is like anesthesia, but it's just like a hundred times more dangerous. And and so then those are the patients that, that, that do struggle. That's right.

So then interestingly, so then as as an anti-aging or as anti-inflammatory concept, then the, the, the one thing would be to potentially just try to start treating people and manage that inflammation and manage that immune dysfunction before, before they get exposed.

Yeah. That's right. And I think that's that explains part of the mechanism. Because, you know there's so called long Covid where people get, you know, the systemic effects and the micro and the line, the clot and the vascular inflammation and kidney dysfunction that, you know, lasts long after the active infection of Covid, even long after they've stopped testing positive.

And that's because of the spike protein. So when the spike protein attaches, it activates platelets. It causes monocytes and neutrophils to stick to the lining of the blood vessel.

That's all information of vascular inflammation. If you give nitric oxide a restore endothelial production of nitric oxide, you completely inhibit platelet aggregation.

You completely inhibit the adherence of monocytes and neutrophils to the outside of the wall of the blood vessel. And you completely mitigate the inflammatory response.

That is mechanistically the only thing that's going to overcome that cytokine storm. When you first get exposed to the to the Covid virus. So that yeah.

And so then it's interesting when so when initially when somebody gets Covid they they're inflammation can happen. And if it gets into the blood vessels and especially with the early versions of Covid right.

The like the wild type and kind of the and probably Delta also there would be an inflammatory situation that would happen in blood vessels. And when that happens, this population is the population that goes down by far the hardest.

But then interestingly, along those lines, then, with long Covid, it's almost like a similar process, but it's the simmering low level vascular inflammation that is, and, you know, there's when we talk about those cells, the monocytes, we're doing some tests where we look at the spike protein and see what the spike protein is.

However, that's not the 100% the total thing, because even when you treat that, it's not 100%. And and what I have found on long Covid is that there's a diversity of things going on there.

And there's vascular inflammation of of probably more than one cause. And so and interestingly, you know, I've seen a lot of athletes that get Covid that end up and they have no exercise tolerance.

But those guys had been pro football players. And you know, do you have a thought on on what the mechanism is of people who were really at 100% health and then they got Covid?

It's it's they seem almost mechanistically a little different to me than the, than, than the metabolic syndrome population. Yeah. Well, look, there's no doubt nitric oxide part of the problem in areas patients with Covid and those with long Covid, but it's not the end all, be all, cure all.

You know, I think what we've learned is that if you have vitamin D levels less than 15 and you get exposed to Covid, there's a good chance you're going to get sick.

So you might have really good vascular function. You got low vitamin D, you're at risk.

Nitric Oxide, COVID, and Immune Function

The other thing, these other micronutrients like zinc and chromium and selenium, you can't elicit, you know, normal cell signaling based on these micronutrients.

You're going to get sick from Covid. So you could have you could be a well-trained athlete. The vascular function. But these other components aren't in check that it puts you at additional risk.

So again nitric oxide is important. But it's not the end all be all cure all. You got to optimize all systems. The human body is incredibly diverse and robust in its response provided that it has what it needs to do the job right.

I love that. So then talk me through. Talk me through how you think about, replacing and and supporting that that whole process in terms of, nitric oxide production.

Yeah. Well, there's, there's two ways the body makes nitric oxide. One is through an enzyme called nitric oxide synthase that's found in the lining of blood vessels in individual cells.

It's found in nerve cells. And it's also part of our immune system. So that enzyme converts arginine to nitric oxide. And you get citrulline as a byproduct.

But you're never and and I think this is important because a lot of people, there's a lot of nitric oxide products on the market that contain arginine citrulline a lot of other nutrients.

The problem is there's never a deficiency in these amino acids. The enzyme that converts arginine to nitric oxide is dysfunctional. So to give L-arginine or Citrulline to a patient within the female dysfunction, it's like putting gas in a car with a blown up engine.

You're not out of fuel. Your engine's broke, so it makes no sense. And in fact, you can push that reaction too far and generate superoxide instead of nitric oxide.

So I tell people you don't need arginine or unless you get, you know, a rare urea cycle disorder called article 16 of gas. And you realize that's the only known human condition where there's a deficiency of arginine.

And then the other, see, if we coupled the nitric oxide synthase enzyme. And that's not as simple as everyone believes. There's a certain redox potential or an electrical potential needed to recover that enzyme.

And so we know how to do that. We put that in our in our product technology. And then the other part of the pathway is through diet, you know, from eating green leafy vegetables, it's the mechanism of action of a plant based diet, Mediterranean diet, the dietary Approaches to Stop hypertension.

It's eating a lot of green leafy vegetables that are enriched in nitrate. The body converts nitrate for the bacteria in the body. Convert nitrate to nitrate, nitric oxide.

So you got to keep the bacteria feed the bacteria that do this. You can do this through eating more nitrate or taking nitrate supplements. Stop using an acids.

Allow that conversion in the acid environment. The stomach. And then when all else fails and Matt, you and I, both the, you know, change in lifestyle is the most difficult thing for, for people, especially patients.

With the way medicines practiced here and, well, all over the world now, people, people want a quick fix. They want to take a pill. They don't want to change their lifestyle.

So the easiest way, and really the only way for people to get better is it got to stop doing the things that make them sick and start doing the things that are going to make them better.

And when they don't, when they're not willing to do that, then we have to make product technology that makes them better. So that's where our technology comes in.

If you don't want to change your diet, if you don't want to exercise or can't, then our thought processes, if your body can't make nitric oxide, then we have technology that does it for you.

And that's how we control and dictate the metabolic state of nitric oxide to an orally disintegrating lozenge that generates nitric oxide for. So the that's kind of the simplistic thing.

But again, you have to understand it. It goes back to a very simple concept that people get sick for two reasons. And two reasons. You're exposed to something that you don't need or you're missing something that you need.

So you've got to remove the source of exposure of toxins or infections. Give the body what's missing so your body can do its job, get out of its way in the field itself.

Right. But that's going to the end. So unpack for me what turns on nitric oxide synthesis. Well, there are a number of things, shear stress, like, for instance, when we begin to exercise and we need more blood flow to the coronary arteries, as you know, as anesthesia allergies, the only way to increase, perfusion of the heart is through dilation.

You can't recruit more capillaries because it's fully, fully perfused. So the only way you do that is through the production of microbots. And so we begin to exercise.

There's increased metabolic demand on the heart. There's shear stress in the heart that tells the coronary arteries to dial to make nitric oxide. If they make nitric oxide, they dilate and they meet the increased metabolic demands on the heart.

You can't make nitric oxide. You become stressed, you get a changes in electrical signal, and you fail an exercise that's basically diagnostic for lack of nitric oxide or the inability of coronary arteries to dial dilute.

The other is histamine. You know, when our immune system reacts, we get a histamine response, an increase in blood flow. There's certain wavelengths of light, that will activate UV, will release nitric oxide from metals.

Then ultraviolet light will actually cleave in oh bound assisting bound proteins to glue the film. So that's kind of what stimulates the enzymatic production.

Nitric oxide. But there are a lot of things that disrupt that. You know, oxidative stress, immune dysfunction, inflammation, superoxide production are all uncouple now and lead to endothelial dysfunction.

And that is like this defining thing that wherever there's anything all dysfunction, there's dysfunction that's well, you know, all vascular beds are the same mechanistically.

So if you have endothelial dysfunction in the sex organs and you can't dilate that to get more blood flowing, getting boards, you have erectile dysfunction happens in men and women.

If you can't dilate the coronary arteries but you can't make nitric oxide, you get a schematic heart disease. You can't control and regulate blood flow.

And you have in the female dysfunction, in the the blood vessels in the brain, you get faster dementia. And you can look at this through Spect scans and look at hyper profusion in certain regions of the brain and certain neurological disorders.

But the underlying common denominator in all of those is inability to regulate blood flow upon the. You know, it's interesting if, if you think about it and, you know, those are the same patients that I saw in anesthesia, but those are all the almost the same patient.

So like in the high, you know, when, when, if you're a guy in your 50s with erectile dysfunction, then you got to be thinking that they always say, that's the canary in the coal mine.

That's the first thing that starts to go. But then often those patients are on a spectrum of neurological dysfunction and issues, and often they're on a spectrum of, their other vascular stuff, often high blood pressure and heart.

And, so it's it's interesting to see that. And, you know, it's reminiscent it's almost like kind of a story. And so then, you know, one of the things is to, is to try to take some nitric oxide.

And now, interestingly, you know, in the past it was hard to get that with ox out oxalates because a lot of those green leafy vegetables are in high oxides.

But your nitric oxide lozenge doesn't have active slide. Send it. How did you do that? Well, we we kind of distill it down to the minimum necessarily components to make nitric oxide.

And then to re couple the nice enzymes. So our philosophy is number one if your body can't make nitric oxide we're going to do it for you. But we also got to fix the endothelial dysfunction.

We've got to re couple the nitric oxide simplex enzyme so that your body's ability to make nitric oxide improves. And so it's really very simple. It's it's biochemistry.

But it's also kind of like some energetic components to because there's an electrical potential, you need a redox equilibrium that you need to prevent oxidation of 4 to 2.

And then we couple them off into. So people, you know, historically just throw a bunch of ingredients together and color that nitric oxide product. And 99% of the products on the market don't work because they don't understand the entomology.

And about chemistry to the extent that you can fix it. And that's where I spent more than 20 years in basic science and academia. And understanding that reaction.

Yeah, that's that's awesome. And how long do you think it takes? You know, I take those daily lozenges. I take one of those every day, that you make. How long would you say it takes?

And, the average person, when you do, because you can do some salivary testing, right. To start to look. How long does it take? But they take to get somebody replaced.

Well, I think it depends on the endpoint. So if you're looking at and look we've done probably most if not all noninvasive as well as invasive in the cath lab looking at right and left part.

Yeah. And looking at the response. But the quickest is if you just take an ultrasound of the carotid and we put the lozenge in somebody's mouth within 30s we can start to see the products dilate.

So that's quick. I mean, you don't feel like when I take the laws and I don't feel my carotid dilate and I'll fill my other blood vessels. Finally.

How Nitric Oxide Is Produced and Activated

But, and if you've got, you know, a history of Tias or, you know, stenosis of the carotid or COPD, where you've got really some vascular problems and oxygen exchange issues, those are the people that they take that they see a response within seconds.

If you look at the response to blood pressure, for example, we've done 24 hour ambulatory blood pressure, one. And you'll see you start to see a reduction in blood pressure within 10 or 15 minutes.

That'll last up to, you know, 6 or 8 hours and then stabilize. So I think but that's only if you have high blood pressure. For instance, my blood pressure is about, 118 over 68.

And I take a lot of if you're taking nitric oxide and my blood pressure doesn't change. And that's very important because you only want to lower blood pressure in people with high blood pressure.

You don't want lower blood pressure in people with normal or low blood pressure. Right. That's interesting. You know when you talk about immune problems then there's there's a interesting overlap with vascular stuff.

And then this is this is this happens in the long Covid people. And then this also happens in Lyme and mold and stuff like that. Where people will have something called dis autonomy.

And that basically is this imbalance of basically the fight or flight and rest and relax and, inert aspects of the nervous system. And, and so then like, for example, they'll stand up and get lightheaded.

They call that pots postural orthostatic hypotension. But there's maybe a whole bunch of different variants of that. That and there's a big immune there's like 100% of the time there's some kind of immune dysregulation going on.

And so then because of that I always have that those patients, and if you're one of those patients, then it's be interesting to kind of think about and read about your supplements because I'll, I'll have people take take that for that vasodilation.

And my logic is I'm trying to dilate those arteries going to the brain, to the limbic and to the, the deeper and autonomic structures to kind of basically get them to physiologically turn on.

We also do the cell ganglion blocks for a lot of these people. And then we will we'll give them nitric oxide lozenges before we do that so that we can kind of optimize the when we open that side effect of that injection is that it dilates the, the, the carotid artery and, increases blood flow to the extent that they get a headache.

But then once I started giving everybody, the lozenges, people tolerate it better. Well, I think, you know, as you know, there's receptor sensitization.

And you'll see this in a very small portion of the population. And you see it primarily in patients who are taking organic nitrates like nitroglycerin or ices or.

But so those people have had so little nitric oxide for so long, they get an upregulation of an enzyme called soluble going like cyclic. So when when you hit them with a lot of nitric oxide, whether it's through organic nitrates within the lozenge, you saturate those receptors and you get massive vasodilation.

But then as you continue, you know you're down regulate those receptors. So that's that's kind of the desensitization that you'll see. With that. I think it's probably the same with with that acute phase dilation.

These people have been sick. They upregulate their second messenger system because they're so low in nitric oxide. But then once you start to repeat and restore nitric oxide, those receptors will be sensitized and downregulated.

And then there's no, you know, headaches or cerebral increase in cerebral pressure or anything like that right now, that the headache is a side effect of the stellate ganglion block.

But when we do the nitric oxide, it seems to be less it seems that certain balance balanced above what happens when you give the nitric oxide. When you do the cath that you'll see, you'll see increased blood flow basically.

Yeah. You know, that was one of the questions we had early on in, patients with coronary artery disease is to prevent, know, coronary steel, you know, this phenomenon.

And so we want to when we dilate blood vessels, we don't want to cause of coronary steel. And so that's what we investigated in the cath lab looking at your left heart hat.

Then we were looking at, you know, in heart failure patients with preserved ejection fractions and trying to look at reduction in pulmonary pressures on the right side of the heart.

And so, number one, from a safety standpoint, we don't see any coronary steel with the technology. Number two, even in patients with F for pulmonary hypertension you can start to see a reduction in pulmonary pressures within ten minutes of taking the lozenge.

And it's unlike giving, you know, inhaled nitric oxide where you can drop pulmonary pressure. But when you turn the gas off you see a rebound effect or maybe of an over, shift of pulmonary pressures where this it's seen that with the, with the laws and you reduce pulmonary pressures and you get a sustained effect.

So it's not like when the logic is completely gone that the pressures go back up. We only had 20 minutes in the cat lab in the study, so we don't know a lot about the long term effects of that, but it certainly lasted 20 minutes long after the loss.

And to fully dissolve it was interesting. The, that was something that we would do in nitric oxide for pulmonary hypertension. And I bet it's interesting because that's another one to think back this way.

When I was at UCSF, the we didn't have another way to get somebody nitric oxide at that time. You know, it's kind of interesting. Yeah. You have to give it the, the, the nasal cannula inhaler.

Right. Yeah. Yeah. The for it for the, for the cardiovascular piece of it, if you had, if you had somebody and they had let's say they're, you know, I have a patient.

I'm just thinking of who I is, is a, family member of one of my patients. And so we just got the call, and I've been kind of worried about them for a while, but we just got the call.

Oh, he's going to have, You need to have either a, cath, which is basically they stick a catheter and into the heart to try to open up one of the blood vessels or maybe open heart surgery.

And so they're sorting that out. And so then this is, this is this would be in a, in a setting of, of, you know, coronary artery disease with probably a little bit of metabolic syndrome.

So when you if you could outline 4 or 5 things of how you think about that and how you would, how you would, try to work with that from a nutritional and a nitric oxide perspective, what would you say?

Well, certainly they gotta change their diet. I mean, I think it's clear you get the in the work of, Doctor Caldwell Esselstyn shows that, you know, plant based diet completely reverses coronary heart disease.

But that's an extreme measure, right? You got to completely change your diet and lifestyle. Most people aren't willing to do that, but I think it's clear from our published data, clinical data on the how nitric oxide is.

You can see plaque regression. You can see perfusion and dilation of the coronary arteries as well as other arteries. And you stabilize the blood. So as you know, it's not about the degree it's to gnosis of the coronary artery.

So you get people with, you know, less than 1,020% to most of the countries that have a am I fatal am I sometimes. So it's they have subtle black, but that part is unstable.

And soft and it ruptures and cracks in. Am I where other people have lived with 90% of the coronary arteries, but it's it's stable plaque. And if you don't have a a risk of it rupturing and causing an acute MI, but you still got to increase the perfusion through, that's the Nordic blood vessel.

And the only way that I know how to do that is through restoration of hypoxia. You can give an exercise upstream, but you have to restore the function of the endothelium of that to prevent more immune cells and platelets from sticking to that existing plaque and also stabilize that plaque.

It becomes unstable. And probably in that patient, you know, exercise is not going to be an option for him because he's probably exercise intolerant, especially with the underlying metabolic issues.

You know, I think mechanistically, we know the nitric oxide will improve the insulin signaling. We've seen a reduction in hyperinsulinemia and hypoglycemia with the nitric oxide.

And then you perfused the coronary artery. But obviously he didn't get there overnight. And he's not going to revert back to normal overnight. This takes time.

Yeah. It's it's it's interesting though that because I've got a couple other people that are kind of coming to my mind that we had somewhat of a, you know, coming to Jesus conversation around, okay, let's, let's really do this.

Let's really, let's really change your diet. The and, you know, the, the, the blood sugar piece is, is that I think there's this, this and the theory also, this is the lining of the blood vessel.

And then there's a blood sugar piece. And those are those two. If you got both of those problems, that's a huge problem. And and so then managing that, that's interesting that, the how long do you think it takes being on nitric oxide?

Those people start to experience a little bit of a blood sugar. And have you have you had anybody tracked the nitric oxide with the continuous glucose monitor where they can they can track and see we haven't we published this in diabetic Animals?

I think in 2009. And we treated them. I have to look back at the publication either two weeks or 30 days. But, you know, there was a statistically significant reduction in both insulin levels and fasting glucose levels in these animals.

And then we brought it back to mechanistically when it said that, you know, it's it promotes blood for translocation to improve glucose uptake. When you get the nitric oxide.

But I don't know if it happens within a couple of hours, a couple of days. I just knew in our experimental model in the lab we could do it within 30 days.

But I think it's a good experiment to do in humans. But now, with this continuous glucose monitoring, it'd be a cool experiment to do. And so basically for people out there, you can, you can call us or go to, your doctor and they can they put a little patch on and then you just put your phone up and it just tells you what your blood sugar is.

So like, if you have to stick a needle into your finger, you're thinking, I don't think I'm gonna check my blood sugar right now, but if you can just go like this and then do it, then, then you can begin to track it.

And so then that's one of my number one things I do for this whole population of patients with cardiovascular stuff, because then we're trying to make it easy for them to get data.

And they always say, and Silicon Valley here, they say he who has or she who has the most data wins. And and so then if you we're trying to get you that data on your phone so that you can start to make those kind of lifestyle choices and make those make those easy.

Well, that's empower.

Cardiovascular, Blood Sugar, and Sexual Health Benefits

And I mean people, people need to be responsible for their own health and wellness. You can't wait till you get sick to go to a doctor and then expect the doctor to prescribe appeal and and change your health.

Let's just think the past 50 or 60 years and modern medicine has proven that that model does not work. You gotta make some fundamental changes. And if you can be proactive and understand these issues or changes based on

lifestyle or diet, and then you proactively make those changes, then you can do what I think everybody's trying to do in medicine, and that's actually prevent disease, not try to treat disease but actually prevent it.

And we understand today the mechanism of most, if not all chronic diseases that we should be able to prevent a lot of these. Now in terms of, blood vessel health, then one of the one of the sort of the popular ideas, you know, in the last few years has been, you know, everybody got into, and had as a, as a supplement what what's your, what's your thoughts about nad as that and in terms of vascular health.

Well, I think it's critically important. I mean, it's one of these things that it's a necessary cofactor in a number of different biochemical reactions, not only for the, you know, in mitochondrial function, but, you know, we use NAD, which is a critical cofactor for nitric oxide production.

It's required for binding, as a cofactor to make nitric oxide. So it's just a phosphorylated form of energy. But again, if your body, because of normal metabolism isn't producing enough or there's not enough flux of NAD to these reactions and you become deficient, things break down.

If you give back what's missing, including inside the body response. So I think it's again, it fits this paradigm that, you know, your body is exposed to something that it doesn't need, or it's missing something that it needs.

And if you give back what's missing, the body responds right. This is sort of like my, you know, we we have this idea of these essential vitamins and minerals and that they're, they're crucial for, for health.

And, and so you talked about vitamin D and, and so then there's, there's a whole bunch of, but then and, you know, any there's just a derivative of B3, but if it's crucial for the function and every cell and, and I think part of the reason I wanted to have you on here is I think magic Oxide is, is like, an essential, an essential thing that you have to get.

Right. And if you don't get it right, you could do all of the peptides, all of the all of the stem cells in the world. And then you may still have a fairly substantial problem.

Now I say, like I obviously have a huge bias, but I think it's corroborated by, you know, 30 years of research that your body cannot. And will not heal until you restore the production of nitric oxide.

I think that's clear. But until then, you're going to you're not going to get perfusion to whatever organ you're trying to fix, and you can't deliver nutrients or other stem cells or other things deployed either either here or systemically to an ischemia.

Morgan, you have to open up the blood vessels and prevent the inflammation, oxidative stress and immune dysfunction in that vascular bed. In order for that organ to heal.

And so we were talking about, you know, immune problems and obviously there's immune peptides. But then there's stuff that would be kind of an almost like a small molecule category like, nitric oxide.

And so then there there's a diversity of ways we think about it that we're another area. We think about peptides for sexual health. But sexual health, probably nitric oxide.

It's going to be one of the biggest factors. You have what what's been your experience with people with erectile dysfunction who start taking regular supplementation?

Well, interestingly, number one was we saw people had their there's three main responses we saw when we first launched this more than 12 years ago, ten years ago, 11 years.

Number one was better energy, better sexual function and better sleep. Obviously better energy comes from better mitochondrial function. Better sex comes from better perfusion of the sex organs.

Better sleep. I still mechanistically I don't know how to explain it, but you can you get an understanding based on

drugs like viagra right, that have been on the market now for more than a decade, a couple decades.

And these these drugs are called phosphodiesterase inhibitors. And so they're not nitric oxide down is there was a so called medical expert on major news couple of weeks ago talking about that being nitric oxide.

Don't that's not the case at all. These drugs potentiate the effects of nitric oxide. And what we've learned from the vascular effects of erectile dysfunction is that 50% of the men that are prescribed Viagra or Lipitor and or the other Ed drugs don't respond, so they don't respond with better symptoms of BPH, and they don't respond with better erections.

Why is that? Well, you need nitric oxide to activate cyclic GMP production. And these phosphodiesterase inhibitors prevent the breakdown of psychology of.

So that particular vascular bed in that patient doesn't generate any nitric oxide. There's no cyclic G. That's cyclic GMP that's being produced. So you can't prevent its breakdown.

So the drugs do not work. We did a clinical trial probably 7 or 8 years ago where we took non-responders to Pde5 inhibition therapy, gave them our nitric oxide.

And we saw an improvement in both symptoms of BPH, urinary urinary scores and better erections. So that's very important because it tells us that 85 inhibition therapy doesn't work in patients because they don't make enough nitric oxide.

And then if you can titrate up the nitric oxide, improve their nitric oxide levels, you can take non-responders and make them responsive. You can titrate down the dose to mitigate the side effects.

And then everything works better. So erectile dysfunction is clearly endothelial dysfunction and a symptom of nitric oxide deficiency. It's very clear.

That's been that's been my experience. And so then with you know another thing we do for that one is we do the shockwave therapy. And I I've noticed that the shockwave therapy works a lot better if people are taking nitric oxide.

And then I've also noticed that the erectile dysfunction medications work better when, when people are taking it. And there's a part of me that that would say, you know, just mechanistically, we're always thinking about those deep brain structures because we see so many immune patients with with dysfunction, autonomic dysfunction or emotional limbic dysfunction.

And a lot of those people have sleep trouble. And there's a part of me that just wonders if the reason they're sleeping better is that they're there's vaso dilating the blood vessels that are going to the brain, and then that makes the brain healthier.

And so then it's easier for the brain to fall asleep. I mean, that's like in simple terms, but right now it makes sense. I just don't know if it's through, you know, more production of melatonin or other, you know, peptides or neuropeptides that are controlling sleep.

I just have never been able to pinpoint it. But yeah. Look, if you refuse any improvement in profusion of any organ, it's going to perform better part of the function of the brain is to, you know, mediate sleep patterns of sleep.

Now, just so you know, as people research it because there's a you've had a pill and then you've had a lozenge. Can you tell me a little bit about the difference between those and when would somebody take one versus the other.

Well, you know, we evolved just like the science. And so we've understood, you know, that, different people need different things. But there's no one size fits all for anybody.

Right? I mean, we think that nitric oxide is critically important. And no matter what the underlying cause of nitric oxide deficiency, we know the lozenge overcomes that because we're not the we control the chemistry of that.

There are other people that can just stop using mouthwash, stop using fluoride, stop using antacids, and their body heals to the extent that they can improve their endothelial function.

And then other people can't or are just addicted to mouthwash or can't get off antacids because of, you know, reflux disease or something like that. So they eat and try to eat more vegetables.

So we published in 2015 that there's as much as a 54 difference in the amount of nitrate consumed from celery bought in Dallas and Chicago versus celery bought in New York.

So you cannot make you don't know. People cannot eat enough vegetables, especially organically grown vegetables, to get enough nitrate to make nitric oxide.

So then what we did is we created a standardized nitrate capsule that if you want to try that, instead of eating 150g of spinach in Dallas, you can take two capsules and get enough nitrate of that spinach.

And then that primes the bacteria, the nitrate reducing bacteria. It works as a prebiotic. So it gives these bacteria substrate to work on. So you wake them up.

Now you're able to utilize nitrate that comes from the diet, as well as nitrate that's formed from the oxidation of nitric oxide. And so that gives you kind of an in people can interrogate each step of the system and figure out what works for them.

So what I do is I try to eat a balanced diet, physically active. So those things work for me. But I still take my micro outside every day, especially when I'm traveling and eating on the go.

So I take the standardized nitrate supplement to keep my levels up, and then I take the lozenge. You know, when I'm feeling run down or before I go to the gym to stimulate nitric oxide or to give my body kind of that boost of oxygen.

And then the other, you know, some people can just, you know, again, just exercise, get sunlight. If you eat a good diet and you're not exposed to a toxic environment, you don't need to supplement anything right.

But nobody lives in a sterile, nontoxic environment, including the foods we eat. So we almost have to supplement because it's not just about nitric oxide, but a lot of the foods we eat today are deficient in magnesium and iodine.

Selenium is most so you you almost have to supplement now. Another thing that I have become a incredible fan of is the cream. Obviously. Speaking of cream, I noticed cream.

I just had cream because I see the Wu-Tang clan behind it, which is kind of awesome. But tell me a I always like to get a music reference if I can, and every podcast, but, tell me about that one, because we are we that's my favorite esthetic, thing that I've, I've actually literally ever found. Yep.

Well, you know, kind of my claim to fame is we know how to make nitric oxide. And then when you start thinking what other utility is there for nitric oxide?

And just like the dermis, the skin is an organ similar to the heart has functional cells. It has to get sufficient blood flow to those cells. And so aging again, whether it's an aging heart, aging brain, aging skin there's a loss of nitric oxide.

So what happens to the skin when you don't get enough nitric oxide. You lose collagen. You lose hydration. Cells don't turn over to regenerate. You get fine lines and wrinkles get dermatitis.

You get an age spot. So I thought, okay, if we could make a topical nitric oxide that we can apply to the outermost dermis and open up those capillaries, perfused those cells, then the skin should regenerate.

We should have cellular turnover. We see collagen deposition. We see fine lines and wrinkles go away.

Topical Nitric Oxide for Skin and Wound Healing

It's anti-microbial. So people with, acne, it kills the bacteria in the pustules. And it's just a great product we see we see amazing results. I think we have four published clinical trials on that.

And in fact, for the drug company, now we're about to submit an investigational new drug application for diabetic and pressure. Three, because we've seen we've got some pretty impressive data on the anti-microbial, the antibacterial effects of it.

We can kill things like, Pseudomonas, staph, a lot of these, bugs that are inherent in infected wounds. And then, as you know, to heal a wound, you've got to kill the infection, and you've got to get blood flow to the wound.

That's the reason diabetic ulcers don't heal, because there's poor blood flow and there's always an active infection or an open wound. So when we apply the topical, we kill the infection.

We get a hypertonic response, we get granulation of tissue, and you heal the wound. So it's been remarkable. And I think, you know, there's been no innovations in wound care for the past 50 years.

People are still treating wounds the way they did 40, 50 years ago. Negative pressure. And then, you know, trying to kill the infection. We do both of those with a single topical, but for esthetics, as you mentioned, you know, the product that's on the market now is a cosmetic product that we're seeing great results with it.

But again, it just goes to show you the power of nitric oxide. When your organ is deficient it becomes dysfunction. That's the outward appearance of age.

And we can overcome it. I, I always like to say the if you find something that works really well in terms of health, for somebody that's really sick, it, well, it will help somebody who's healthy be healthier.

Because things that, if, if somebody is really sick and you have to have a really good product for them to be able to take it because it filters them at all, they could get worse.

So it's kind of a nuance to to finding those things that you can do for that population. So that by analogy is kind of a similar where you say if there's something that you can put on a diabetic wound to make it better, it probably will make our face better.

And I noticed that, you know, you told me, yeah, this is just kind of crazy, but you did tell me that it's anti infection. And then I had a couple of happy patients with, herpes outbreaks.

And so then they put it on the herpes outbreaks. But generally and on the face and they got it helped them. We did other things as well. But they're like that that helped kind of right away, which was which I found surprising.

And so then this is basically you take two ingredients, there's a of a pump and you do one pump and then the other pump, and then you mix them with and then you rub it on your face, or you can rub it on other parts of the body.

What what's what's happening with that, with that reaction. When you do that? Well, I don't know if I've mentioned it, but nitric oxide is a gas. It's a gas under normal atmospheric temperature pressure.

So to create a gas this bioactive is a challenge. Right. And to make a solid dose form of a gas, it's kind of the code we cracked years ago. So to make this gas you got to create the two separate components.

And if you combine them in create this gas you get a a nice bomb. Right? We don't want to create bombs. So we have to keep these these things separate.

And so when you mix them together the chemistry comes together and you generate nitric oxide. Yet so this is a very deliberately and strategically designed.

It's pH balanced in both chambers. And then when you mix them together the combining pH is about 5.5 to 6, which is the pH pH of a healthy dermis or at only the skin.

And so when you do that the nitric oxide gas is produced, diffuses in all three dimensions. So above it. And we can detect that with an oxide analyzer that is the fuze into the dermis into the skin.

And there's a limited diffusion. So it's not going to diffuse into deep into the tissue and and dilate you know resistance or it just won't diffuse that far in the tissue.

But it will diffuse several millimeters in and and open up capillaries, dilate superficial blood vessels and lead to an increase in blood flow or high premium to that area.

And so when you flood that area with oxygen and nutrients and you get better hydration, you get collagen deposition, you get the good stuff and the bad stuff.

Cells turn over and you get cellular regeneration. It's really that's a and and we've we have had people use that sort of from an esthetic perspective for their face.

I've also had people who have erectile dysfunction who will use that either or, but both men and women, have used that topically on the genitals. And they've said they felt kind of an improved blood flow.

And, and we've had some positive feedback. Have you, have you guys heard that also? We have you know, obviously we can't make those claims. But, you know, I tell people it it gets the wrinkles out and you can take it, you can apply it to wherever you want to increase blood flow.

So it works the same. But, you know, we've marketed as a cosmetic, you know, as a physician, you can use your best medical judgment to give patients what you think is going to be best for their outcome.

But now we have even thought about calling a drug application for that specific use, because we have seen an improvement in both men and women. Now, the challenge is to get it to where you can deliver that nitric oxide deep enough in the tissue to dilate the corpus cavernous, the main conduit artery into the penis.

Final Thoughts and Resources

And the technology we have in that cosmetic product will not allow the fuze toxic gas far enough into the tissue. Now, for the women, the blood vessels are a little bit more superficial in the clitoris to get engorgement.

So we found that it works a little bit better in women just because of the superficial nature of the blood vessels that supply that are working, as opposed to me.

But that said, basically, that encapsulates almost our whole conversation, which is this, that we have to we have to think about blood flow. We think up to think about where that blood flow is.

For somebody like me, I'm trying to combine some combination of interventional things with injections of peptides or injections of other things to basically we're kind of constantly trying to address nerves or arteries and blood flow into blood and into vascular beds.

And then we're also in parallel to that, thinking about what's happening at a cellular level inside the capillaries. And so nitric oxide is at some level implicated.

And all of that. And so it's kind of amazing. I'm delighted, that we got to cover all of this stuff. And, one, one quick hour. It's awesome to talk to you.

Any final thoughts for people? You know, for your audience and listeners, I think, you know, it's important to do your own research, understand nitric oxide, and how important it is on the body, and then just make those simple changes.

And your body will thank you for it. And, you know, I've got an educational website, doctor Nathan s bryant.com. I do a monthly blog. I try to make it timely and practical and in terms of, you know, hopefully provide some information that people didn't know prior and they can make some very simple steps in their life and see the improvements.

Awesome. Well, it's great to have you as a friend. And it's it's great to be educated by you. And, thank you for what you're doing because you're making the world a healthier place.

I really appreciate it. Well, thank you, Doctor Cook. I certainly appreciate you and your friendship and, all you're doing to make people better. All right, well, have an awesome week.

And, try some nitric oxide people.