Nitric Oxide - The Future of Regenerative Medicine

Michael Karlfeldt, ND, PhD with Nathan S. Bryan, PhD

Michael Karlfeldt, ND, PhD
Dr. Bryan. I am so excited to have you on this segment of a Regenerative Medicine Summit and we're gonna be talking about some pretty kind of groundbreaking things that a lot of people are not aware of and I'm really excited about it.

Nathan S. Bryan, PhD
Thank you, Michael. It's great to see you.

Michael Karlfeldt, ND, PhD
Well let's kind of let the audience know all the things that you've been involved in. You earned your undergraduate Bachelor of Science degree in biochemistry from the University of Texas at Austin and your doctor degree from Louisiana State University School of Medicine in Shreveport, where you were the recipient of the Dean's Award for Excellence in Research, pursued your pie host doctor training at the Kirsten fellow at Boston University School of Medicine in the Whitaker Cardiovascular Institute. After two year postdoctoral fellowship in 2006, you were recruited to join faculty at the University of Texas Health Science Center at Houston.

And by Faried Murad, you said 1998 nobel laureate in medicine or physiology, Dr. Bryan has been involved in nitric oxide research for the past 20 years. So a long time and we're just now finding out about it pretty much and I and has made many seminal discoveries in the field as many seminal discoveries have resulted in dozens of a issued us and international patterns and the product technology resulting from his discoveries and inventions has improved patient care worldwide. Dr. Bryan is a successful entrepreneur and founder of a human n inc and also new mo nitric oxide LLC and nitric oxide innovations LLC and Bryan nitrous ooh tickles LSC is product, technology is responsible for hundreds of millions of product sales worldwide. Most recently, Dr. Bryan serves as founder and CEO of nitric oxide innovations, L. C. Privately held clinical stage

biopharmaceutical company that is actually engaged in the discovery development of nitric oxide therapies and their lead drug candidate and no virus and no virus. It is currently in phase three clinical trial for the treatment of Covid 19 in African Americans and Hispanics Dr. Bryan is an international leader in molecular medicine and nitric oxide biochemistry. You have been busy,

Nathan S. Bryan, PhD
It's been a journey for sure.

Michael Karlfeldt, ND, PhD
Yeah. Oh wow. So how was it to work? I mean here you have somebody that's won the Nobel prize. I mean that's I mean and how was it to work with such a gentleman? I mean that that must have been incredible.

Nathan S. Bryan, PhD
Well, you know, it wasn't really an electric atmosphere. You know, you learn a lot from people who are innovators and have made really world changing, life changing discoveries and so I think, you know, it's contagious and and so it's passed on but you know, they knew long ago that nitrous oxide was important obviously in 1998 Nobel Prize was awarded. So, you know, they discovered the importance of nitric oxide and how it's produced in the body. You know, and I've kind of created a name for myself and become famous for creating a solid dose form of this gas that actually replenishes and replete nitric oxide inside the human body. So it's really it's been an honor to continue the science and really to advance it to a stage where we can actually apply this in clinical practice.

Michael Karlfeldt, ND, PhD
Yeah, it was incredible. And nitric oxide before 1998. I mean, what kind of role did it have? I mean, did we even think that it played a role in the body?

Nathan S. Bryan, PhD
You know, even then? You know, it was recognized that it's the molecule that's produced in the lining of the blood vessels that regulates blood flow and circulation throughout the body. So it was at that time considered a vaso dilator, meaning that it opened up the blood vessels and improves circulation and auctions but fast forward, you know, 2025 years, we now know that it's much more than Aviso dilator. It's what controls, you know, protein structure and function and oxygen delivery and glucose uptake and exercise performance and mitochondrial biogenesis.

It's responsible for mobilization of our own stem cells. Which is obviously extremely relevant and important for the regenerative medicine summit. It's responsible for the prevention of the telomeres, the ends of the chromosomes that get shorter with each cell division and basically predict lifespan. So everything we know about longevity and wellness and really the metrics of life of how well we live and how long we live revolves around the production of nitro toxin.

Michael Karlfeldt, ND, PhD
So, for people listening, I mean, obviously you're thinking then, well, how can nitric oxide? How can this improve my life? I mean, how is that going to impact me? And it sounds like it kind of bleeds into so many things. So what would you say to people out there that this is the reason why you need to really pay attention to nitric oxide? I mean, you I want to go into all these different things that you kind of read off that it does because all these are huge subjects, but just so that people can relate to it a little bit better.

Nathan S. Bryan, PhD
Well, the kind of the broad kind of take home messages your body cannot and will not heal or perform optimally without nitric oxide. So if you want to perform better, if you're like, you know, you and me and we're healthy and you want to stay healthy, the nitric oxide is extremely important and allowing your body to prevent the onset of progression of disease. Or if you're sick, like most Americans are trying to get well when medical treatment has failed you, the nitric oxide should be the solution you're looking for because every major chronic diseases characterized by loss of nitric oxide production and when you lose nitric oxide, what happens when you lose regulation of blood flow.

So you have low blood, low circulation for circulation? You have inflammation, immune dysfunction, oxidative stress. Those are the hallmarks of every single chronic disease doesn't matter if it's cardiovascular disease. Alzheimer's diabetes, autoimmune disease, pulmonary disease, kidney disease. The common denominator in all those is loss of nitric oxide, inflammation, oxidative stress and immune dysfunction. And the beauty of what nitric oxide is and does is it's self correcting. So if we can replete and replenish the production of nitric oxide blood flow improves circulation, improves, improves inflammation goes down. Oxidative stress goes down immune dysfunction is Medicaid. So it corrects every single aspect of chronic disease.

Michael Karlfeldt, ND, PhD
Yeah because obviously I mean we need nutrients and oxygen to get to locations and that's what we have circulation. So if all the highways and all the roads are blocked then obviously we're not gonna get anywhere. So now the cells are starving just based upon that. And then you're talked so we have that component is obviously important and then inflammation. I mean we know inflammation plays a role in and I would say the majority of all diseases. I mean inflammation is just there we look at cancer. Look at aging. Look at M. S. Autoimmune conditions. Look at diabetes like I mean you name it, it's there and then just in the regenerative aspect. Yeah we have the term inflammation you know which we know that we're aging faster when were inflamed. And then you know the mitochondrial aspect the immune system regulation stem cell. I mean, these are huge factors. So tell me a little bit kind of how can a molecule that's just you know, it's just too it's just you know, you know, it's just components to atoms. How can that do so much in the body?

Nathan S. Bryan, PhD
Well, it's a very good question. And that really was kind of what intrigued scientists for many years because it's a signaling molecule, it tells the body what to do from many different aspects. So in terms of inflammation, it basically down regulates the huge in molecules on the lining of the blood vessel and prevents, you know, the vascular inflammation where the monotypes and t cells start rolling and adhering and ex Travis ate through and enlisted an immune response. So all of that is mitigated by nitric oxide. But it's also part of our, you know, innate immune system. It kills bacteria, kills viruses. And so it's a gas that just freely diffuses. So it can go anywhere and basically regulate and signal many different aspects of biology. And we're learning more about how this molecule signals every day every week. You know, there's over 180,000 papers published in the scientific literature. So we know a lot, but there's still a lot we don't know. And so that's what makes this area of research such a, you know a treasure trove of discovery.

Michael Karlfeldt, ND, PhD
So, actually, I mean, and I know you're doing kind of working on a nitric oxide drug in regards to Covid and Covid, you know, we know as a vascular disease where you have kind of that inflammation, that up regulation of the immune system. So, that would be that one of the functions in regards to kind of the monastery sites and they adhere to the lining of the blood vessels. And so if we can regulate that more appropriately, then obviously we will not have these kind of clot formations and we will also not kind of the transport of oxygen through the membrane of the blood vessels will be appropriate, meaning that the tissue are able to get the

oxygen, you know, because it's not inflamed from the immune system attacking the lining of the blood vessels.

Nathan S. Bryan, PhD
Yeah, that's right. So we recognized early on, probably in March or April of 2020 that the people that were getting sick and dying from Covid where the people couldn't make nitric oxide. These were the elderly African Americans with a previous heart attack, diabetes, obesity, smoking, kidney disease, lung disease. So, the problem was when you were exposed to pathogen and Covid is really no different than any other respiratory virus. Right? We attaches to the airway epithelium and then our immune system goes to the site recognizes a foreign pathogen. And then when we generate a lot of nitric oxide, keep the virus from replicating and we don't get sick, but in people who have poor circulation and can make nitric oxide, we don't elicit an immune response. So the model sites don't get to the site of infection or the attachment. The virus replicates propagates throughout the body despite protein causes, vascular inflammation causes platelets to aggregate and up regulation and the timer

And you get systemic disease. So every aspect of ideology about COVID-19 can be explained by simple loss of nitric oxide production. So it made sense to us. If we can initiate early stage nitric oxide therapy within 72 hours of onset of COVID symptoms or exposure, then we can prevent this whole proliferation of disease, prevent the loss of blood oxygen saturation. Keep people out of the hospital, keep them off the mechanical event. If you can do that, you can keep people alive. And that's exactly what our drug study was showing for the past two years. But to the console, those are the really sick people. You know, I'm probably the best example of how our immune system deals with respiratory virus. So obviously I've been exposed to Covid, I've been on an airplane every week since probably June of 2020 26 clinical sites for a Covid drug study. So I don't wear a mask. Typically unless I was absolutely forced to.

But yet I've never had covid. So it's I've never been sick from a viral infection in more than 20 years. So we're exposed to viruses every day, respiratory viruses, seasonal influenza COVID-19. But if your body is primed and your immune system is functional and your circulatory system is functional and your body can generate nitric oxide, then our immune system deals with it and it kills it at the site of infection. It nips it in the bud and it doesn't propagate throughout your body and you don't get sick. So this is exactly how our immune system is designed to work. So in this obviously there's no need for vaccines. There's no need for any type of M. RNA genetic manipulation. You just gotta allow your immune system to do its job.

Michael Karlfeldt, ND, PhD
Yeah because it's obviously the key is the the appropriate immune modulation, meaning that you rely on the intelligence of the immune system and by doing that you want to give it the maximum amount of tools that need to be able to function efficiently and and like you're mentioning is that covid, you know, that are the extreme cases you end up in the hospital, you know, put on the ventilators, you know, so that is kind of an extreme but we are just like you in your situation, we are exposed to these all the time and how our immune system is responding to. It determines whether we are put in that kind of inflammatory state with immune system is hyperactive, maybe not to a disease state but we're kind of in that inflamed hyper inflamed state that promotes aging or promotes like an autoimmune condition. But if we can then kind of make the immune system more efficient, clear out the virus and then also then tell the immune system you don't you don't need to adhere to these places and calm down. You know, we got this then then we don't have to worry about these other conditions that are are in themselves becoming pandemics, you know, like all the autoimmune and so forth,

Nathan S. Bryan, PhD
Yep. Now look at whether, I mean obviously we've learned a lot over the past three years about the role of micro cock said in our immune system and infectious disease, but it regulates every aspect about health and wellness. So if we can just simply restore. So number one, we gotta figure out and we discovered this many years ago how the body makes nitric oxide, what goes wrong and people that can't make it then how do we fix that? So, you know, we can have we can very proudly report now that we know the answers to all these questions. So now the question is really the challenge is how do we get this in the hands of positions and healthcare practitioners so they can apply it into their clinical practice because, you know, I'm a basic scientist who does research and discovery, but this research and discovery means nothing if it never reaches patient care and the people on the frontline treating patients seeing patients every day, we have to be able to translate these discoveries into clinical practice and I think that's why this is so important and what you do and other clinicians and really trying to educate the community at large on the importance of nitric oxide.

Michael Karlfeldt, ND, PhD
And so and I want to kind of get into get into that a little bit more later on. But so but I really want to kind of establish that people really can understand the value of nitric oxide and why it's so needed. So obviously, I mean heart disease cardiovascular disease is the number one killer. And if we can then keep our blood vessels healthy then you know, which is nitric oxide plays a

tremendous role in that aspect. You know, not only as a vice vaso dilator but then reducing the inflammation along the blood vessels which will then reduce the need for plaque and author sclerosis and all these things to kind of build up because that is just as a response to the inflammatory condition along the blood vessels. So it can control that inflammation with nitric oxide does. Then there's less need for for the build up and also then obviously we won't move towards heart disease in any shape or form. So we have that component and then also for the immune modulation. You know, we we have that as well. But then we have things like you know, you talked about stem cells and then also things like neuro transmission, you know where you have a neurotransmitters in the brain you know with people dealing with. I mean stroke and all of that makes sense you know because of the circulation. But then also things like Parkinson's and A. L. S. And and all things that has to do with neurotransmitters being appropriately you know sent between gaps you know from one nerve cell to another. You know it plays a role in those areas as well, correct?

Nathan S. Bryan, PhD

No. Absolutely. So you know in order for cells and tissues to function you have to get the good stuff in and take the bad stuff out. So there's a vascular component to every major chronic disease. And really I like the work of Dr. Daniel Amen because he's shown very clearly that all brain disease neurological disease is characterized by reduced blood foot. So whether it's Parkinson's A. L. S bipolar, chronic traumatic encephalopathy from post concussion or vascular dementia and Alzheimer's there's a disruption in the blood flow to certain regions of the brain. And when you can't when you don't confuse those regions of the brain then you don't get these neurotransmitters released. You get this regulation of the communication and develop neurological symptoms. So if you can restore blood flow, get the oxygen the nutrients, the amino acids, the signals you need to neuro transmission and then you can take out the metabolic waste product then the human body heals itself, it does its job and everything takes care of itself.

And I think that's why mo well all Alzheimer's drugs have failed because these drug companies are going after the consequence of disease rather than the cost. The beta amyloid plaques and the tangles of Alzheimer's are consequence of insufficient blood flow. So you get build up of the metabolic waste. These present as tau tangles and amyloid plaque. So it's a consequence of disease. It's not the cause of disease. And that's why these drugs fail. What we do is completely different. We understand the ideology of disease to the extent that we can fix it. We understand the root cause we improve vascular blood flow, oxygen, nutrient deliveries every cell in the body. And then the body's regenerative by nature. We mobilize stem cells. You can go and replace and

replenish dysfunctional cells and we regenerate. I mean that's so aging is really not. It's you know, we were wearing ourselves out every day, right, aging is just the inability to repair and replace dysfunctional cells that's controlled by our own stem cells which are controlled by the production of nitric oxide. So if we restore nitric oxide, the stem cells get the signal, we go and replace and replenish uh dysfunctional cells and we regenerate. And yet we don't age. At least we can't do anything about the chronological aging process. But we can certainly do something about our biological age.

Michael Karlfeldt, ND, PhD
Yeah. And the key is I mean we are living longer now than we used to, you know, throughout history. And so, but the issue is that because we are living longer, we're than dealing with a lot of these diseases that are related to aging. So now we have them a longer time that we are in essence suffering. You know, because we are not recognizing the need to address these diseases, you know, to connected with aging like alzheimer dementia, any kind of inflammation, cardiovascular arthritis, you know, all these things. So, it is then important to really recognize that you need to start to kind of take care of yourself early and recognize the importance of blood circulation. And you shouldn't wait until you start to develop symptoms. Because when you develop symptoms, that means that the body is trying to compensate for many, many years. And then all of a sudden says, I give up, you know, and I'm just gonna let you have it and then you're symptomatic.

Nathan S. Bryan, PhD
Yeah. You know, unfortunately, that's how Western medicine is. Right. It's a reactive approach. So people, people don't make changes until they're in a crisis and always tell people, look, it's much simpler and much more affordable to prevent disease than it is to treat it. So our body is constantly telling us and reminding us, hey, something's not right. And if you don't listen to your body and you wait too late then you and symptoms and disease ensues then it's much more difficult to get better. So it's easier to prevent than it is to treat. So people have to understand that we have to change the way we think and we have to change the way the medicines practice in the US from a reactive practice to a proactive practice. And I think when we do that, when and only when we do that, we'll start will people start to live longer and live better? Because people are living longer now. But they're certainly not living better. They're just living with chronic disease and under the care of you know, a health care system that fails them through drug therapy.

Michael Karlfeldt, ND, PhD
Yeah. And the way the elderly are taken care of is exactly that. I mean they're just dragged down and they're just put in homes, you know where yeah, they're not really cared for that well. And so it is important to do everything that we can when we can when we're as young as possible to make sure that we can increase our health span. We can have our independent living for as long as possible until I mean we are going to die. But let's live well until we do. And that's why something like nitric oxide is such a phenomenal tool in that process. I mean you all almost call it the I mean you call it the most important molecule in the body and and it's because of all this signaling mechanisms, you know, that the intelligence that it brings to the rest of the body.

Nathan S. Bryan, PhD
That's right. Yeah. My dad constantly reminds me and it's a good reminder because I have known I was going to live this long and we're taking better care of myself. Right? So we have to constantly remind that like nobody gets out alive. You know, like my good friend Dr. Joe Maroon says I want to live as long as possible, but die as young as possible. Right? So it's really about our lifespan and how well we live throughout our entire life until, you know, until our day of exploration.

Michael Karlfeldt, ND, PhD
Yeah. Yeah. And you mentioned like the stem cells, I mean, they only they only function so they kind of hang out in our body, but they only functions as well as they are instructed to do, meaning that there needs to be appropriate communication, telling the stem cells that hey, we need help over here and this is the activity that needs to take place and and nitric oxide plays a huge role in that communication so that the stem cells can have appropriate action in the areas that needs to be regenerated.

Nathan S. Bryan, PhD
No, that's exactly right. You know, it was discovered, I think back in 1996 that nitric oxide is the signal that tells our own stem cells to mobilize and differentiate. So, you know, we have stem cells all over our body and our bone marrow and our fat tissue, you know, they're circulating around, they're just kind of waiting for the army that's waiting to get the signal to go and repair and replace and nitric oxide is that signal? So if your body is compromising stability, make nitric oxide. It's not that you've lost the number of stem cells, you've lost the function of those stem cells. So then, and we've published on this, you know, several times in several clinical studies where, you know, you take people with chronic disease or even inborn errors of metabolism and

then we give them nitric oxide, we see a mobilization of stem cells and progenitor cells and they basically repair and regenerate their tissue. Heart disease goes away. Kidney disease goes away, plaque in their blood vessels goes away simply by doing nothing more than restoring their production of nitric oxide.

Michael Karlfeldt, ND, PhD
That's amazing. And so would nitric oxide. I mean, is there because I know with certain hormones they decrease with aging. And because I mean, genetically we are designed to obviously, I mean, we're like a clock that's winding down, You know, So genetically we are designed to kind at some point die. And with that then functions are then slowing down. So as nitric oxide than being depleted or is it less when you're older than when you're younger, is that the case?

Nathan S. Bryan, PhD
Well, there's two ways the body makes nitric oxide. So the first pathway to be discovered was through an enzyme found in the lining of the blood vessels called nitric oxide synthesis. And this enzyme converts argentine to nitric oxide. And we call this endothelial function. So if you have good an ethereal function, then when you're in the cells are stimulated, they can generate nitro toxin when we develop what's called in the feeble dysfunction. That means that when you get a signal or when you stimulate or activate nitric oxide production, the enzyme doesn't work and it can no longer convert Argento nitric oxide. So it's that pathway that becomes dysfunctional with time. So by the time we're 40 years old only makes about 50% of the nitric oxide through that pathway, as we did when we were younger. But now there's a recognized compensatory kind of a secondary pathway that can overcome in the female dysfunction. And interestingly enough that happens through nutrition and die.

And so there's what's called the nitrate nitrite nitric oxide pathway. So you get nitrate from green making vegetables. This molecule is metabolized by World micro by oral bacteria and then we swallow that and it generates nitric oxide gas. So you can overcome in the feeble dysfunction and overcome nitric oxide deficiency from that pathway through Ripley shin through the diet. So what, but what happens is that people have in the female dysfunction and they have a poor diet or they're not getting the nitric oxide produced from the oral microbiome and through stomach acid secretion, then you become globally nitric oxide deficient. And these are the people that have high blood pressure, erectile dysfunction, full blown cardiovascular disease, vascular

dementia, Alzheimer's diabetes, Every major chronic disease we deal with today can be explained by a complete loss of micro oxide production.

Michael Karlfeldt, ND, PhD
So it almost sounds to me that it's kind of a has a domino effect. I mean because you when you don't have enough nitric oxide then your blood vessels, the lining of your blood vessels get inflamed and because they are inflamed you produce even less nitric oxide. So it just has that cascading negative cascade effect where it just gets worse and worse. So it then becomes extreme in order to be able to reverse that. The only way seems to be then through dietary changes and making sure that you maximize and this alternative pathways and through the food that you're eating.

Nathan S. Bryan, PhD
That's correct. And so when we set out to develop novel and innovative nitric oxide based therapies or product technology, our whole premise was if your body can't make nitric oxide then we have to do it for you. So similar to like if you know, the best example is probably hormone replacement and if your body is not producing these hormones because of age related effects, then obviously you repeat them through shots or through creams or trophies or things like that? So that was our philosophy with nitric oxide? If your body can't make it, then we have to do it for you. And that's the basis of our nitric oxide delivery system to do an orally disintegrating tablet. When you put this laws in your mouth, it generates nitric oxide. Guess like it's the only technology in the world that does if your body can't make it, we make it for you. But more than that we understand now the Entomology and biochemistry of the enzyme in the lining of the blood vessel that we can now re couple and restore the function of that enzyme. So we're doing two things. We're providing an exogenous source of nitric oxide that patients typically can't make. But then we're providing the components that re couple the nose enzyme, restore endothelial function. So their body's own ability to make micro oxide is restored and you see remarkable effects when that happens.

Michael Karlfeldt, ND, PhD
So what are some of the effects? Because that's kind of the point that I was making is that it just has this negative downward spiral. And you need something to be able to kind of bring it back so that you can restore that function and then to be able to have a tool like that to restore the function so that your blood vessels can start to produce, you know, the lining is is functioning appropriately so that you can produce in nitric oxide over there. So what are some of the effects

that you've seen? I mean, you know, you sold I mean, what was it? 100 million? I mean there was like millions all over the yeah, it's all over the world, millions of you've done a lot. So what are some of the effects that you're seeing from people?

Nathan S. Bryan, PhD
Well, number one, we see a normalization of blood pressure. You know, two out of three Americans have an unsafe elevation in blood pressure, which is the number one risk factor for cardiovascular disease, the number one killer. So that's a very important. # two, we see a reduction in inflammation. That one of my patents issued patents on the method of lowering inflammation. We see a reduction in triglycerides. And triglycerides are really the components of the lipid panel that are inflammatory. So, total cholesterol, LDL, HDL that none of that all that is meaningless in terms of cardiovascular risk. But it's really your triglycerides. So one of my patents is on a method of reducing triglycerides. We're seeing an improvement in glucose uptake an insulin signal. So, really critically important in insulin resistance and really metabolic syndrome metabolic syndrome is you have, you know, diabetes insulin resistance hypertension and Hyperloop Idema in terms of triglycerides.

So, nitric oxide. It's the trifecta of we normalize blood pressure. We improve glucose uptake and improve insulin signaling. And we lower triglycerides that alone is life changing in terms of affecting a very high risk population for developing heart attack and stroke. We improve exercise performance. You know, we've got products that can allow you to adapt to high altitude uh you know, part of the adaptive response to low oxygen and altitude is to improve micro cock side production to allow you to better deliver oxygen at a lower partial pressure at altitude. So you don't get altitude sickness, you don't get mountain sickness and you certainly don't develop high altitude pulmonary edema, which is sometimes deadly. So every aspect about what we do and what micro oxide does affects every major consideration for chronic disease.

Michael Karlfeldt, ND, PhD
Yeah. And that's huge. And so kind of going back a little bit because I was so fascinated with this other pathway and kind of the for people to understand what kind of food that is important in order to be able to maximize that pathway and what people do normally that will interfere with that pathway to function optimally. So tell me a little bit about that because that is such a huge piece of information for people to understand

Nathan S. Bryan, PhD
Now, it's critical and this is probably the most common jaw dropping response I get when people understand this, right? Because we know that diet can affect many different chronic diseases, right? In fact, I mean diet is probably the most important consideration in all diseases. So what we've discovered is that there's a molecule called nitrate that's found primarily in green leafy vegetables, things like spinach, Arugula, Kale, celery, uh things like that. And then this molecule once we consume these vegetables 90 minutes after we consume it, our body takes it out of our gut and puts it in our celebrate. So now after that meal for the next 68, 10 hours each time we salivate we're secrete ng nitrate And then the bacteria that live in the crypts of the tongue. There's some what we call nitrate reducing bacteria. And then these bacteria Metabolized nitrate in the night strike.

This is a two electron reduction reaction. So now our saliva is enriched in nitrite and I developed a celebrate test strip back in 2010 that can detect celebrating nitrite and the body's ability to metabolize these dietary these these nitrates from the diet. And then when we swallow your own saliva now we get a burst of nitric oxide gas in the lumen of the stomach. So all that fuels endogenous nitric oxide production budgets nitric oxide signals. So what we have to do now is we have to kinda check some boxes at each step of the way. Right? So the first is are you getting enough nitrate from your diet. And we published in 2015 that the standard American diet is deficient in any nitrate. Right? So just as most Americans are deficient and things like magnesium and selenium and chromium were nitrate deficient.

And it's very difficult. Well it's basically impossible to know if you're getting enough because you know in 2015 we published a paper showing that there are regional differences in the nitrate content of vegetables. So whether you live in Los Angeles, Dallas, Chicago, New York or Raleigh and there's much as 100 fold difference in the amount of nitrate in celery for example. So the one we're nitrate deficient number two is two out of three Americans use mouthwash every single day 200 million Americans wake up and use mouthwash and that's destroying the oral microbiome. It's disrupting this nitric oxide production pathway. And people become get high blood pressure. They lose the cardio protective benefits of exercise. They develop sexual dysfunction. And all of that can be traced back to the use of mouthwash

Michael Karlfeldt, ND, PhD
Because you I mean in your you know talking about the bacteria so you actually want the bacteria there in your mouth hole because that bacteria is the one that changed then the night

nitrate into nitrite. And then when we swallow the nitrite it then becomes nitric oxide in the stomach

Nathan S. Bryan, PhD
Provided their stomach acid. And that's what leads us to the next problem. And that's the use of an acid You know there's 200 million prescriptions written Fran acids every year and that's not even counting the over the counter purchases. So these drugs are extremely dangerous. In fact they were never approved for chronic use. But I know people who have been on P. P. I. S. And antacids for 10 12 15 20 years. And now there's clear evidence paper published I think in 2016 That people who have been on an assets for 3-5 years had about a 40% higher incidence of heart attack and stroke. So these drugs are causing heart attack and stroke because they're disrupting nitric oxide production. So now you gotta ask yourself what do I need to do? Right? So if you're using mouthwash you have to stop get rid of fluoride in your toothpaste. Fluoride is an antiseptic it's killing the bacteria in your mouth. It's a neurotoxin and it's killing your thyroid function.

And by the way you got to get rid of fluoride in your drinking water the water coming into your home fluoride is probably one of the most toxic molecules on the periodic table. And yet it's in our toothpaste, it's in our water supply that we're drinking that we're cooking in that we're bathing in. You gotta get rid of fluoride. And then two if you're on an acid you have to you have to get figure out how to get off and ask because your body cannot and will not heal without stomach acid production because it's part of the nitric oxide production pathway. And then you've got to get enough nitrate in your diet. And that's gonna that's a very challenging kind of aspect. And so we've you know, we know how to do this. We've created product technology that basically overcomes all these deficiencies. So when all else fails, you know we have product technology that doesn't for you but we encourage people just to change their lifestyle. Stop doing the things that disrupt nitric oxide production and start doing the things that promote it. They want some more green leafy vegetables, modern physical exercise, 20-30 minutes of sunlight exposure a day or infrared light therapy. And the body started to heal itself.

Michael Karlfeldt, ND, PhD
And that was the point I wanted to kind of here as well. So the infrared helps with the production of nitric oxide. So obviously them being out in the sun kind of a skin exposure to sun helps also them with the production of nitric oxide.

Nathan S. Bryan, PhD
Well it can you know, there's certain wavelengths of light both on the U. V. Side of things. And then the really it's full spectrum infrared that will release nitric oxide bound to. So the UV light will cleave ino bound to assisting five. So that's a covalin volume. The higher energy do that infrared provides a frequency that releases nitric oxide that's bound to metals. Right? So there's it depends there's a limited diffusion of those wavelengths into the tissue whether it's direct sunlight exposure. What's whether it's infrared. But the challenge has been or the consideration is you have to have these photo label stores in order to be released by life. But in people that are nitric oxide deficient, there's less nitric oxide. So there's less nitric oxide down the tiles or less nitric oxide down the metals. So there's less nitric oxide to be liberated by life there. So what we found in a number of clinics that use light therapy or red light is if you pre treat these patients with nitric oxide and then exposed them to infrared light therapy, you're gonna get more clinical benefits of the light therapy because we've traded up these photo label stores and when you hit it with light you're releasing a lot more nitric oxide than you would have. They not re pleated or tight traded up these these stores.

Michael Karlfeldt, ND, PhD
And yeah, the P. P. I. I mean it was fascinating so that people kind of recognize that. Yes, I mean I'm dealing with acid reflux or GERD or whatever it may be. But if I'm on these medications then I'm 40 you said 40 per More likely to have, you know, a stroke or a heart attack.

Nathan S. Bryan, PhD
Not more likely these are actual heart attacks and strokes.

Michael Karlfeldt, ND, PhD
These are okay, so this is your 40% you will have 40% more risk

Nathan S. Bryan, PhD
40% increase in actual events. It's crazy. I mean it should alert the FADA to take these drugs off the market similar. They did the Vioxx and celebrates back in the early 2000s. There is clear evidence that this is increasing the incidence of heart attack and stroke. There should be a black box warning on these drugs. They're very dangerous and they're never been approved to use chronically.

Michael Karlfeldt, ND, PhD
And obviously if you then change your diet because a lot of times the garden acid reflux you know tends to not be due to that. You have too much acid in the stomach. But it's because it's too little. And so if we then support the production of hydrochloric acid then you are then less like to deal with the guard or deal with acid reflux and then you are less likely to have to be on these P. P. I. S. And then you're less likely to then deal with these kind of cardiovascular events and I mean who wants to have a stroke? I mean I'm okay if I just go and die and just kind of that's it but I don't want to have a stroke and be paralyzed and be nonfunctional. And I mean I just don't want to go there you know

Nathan S. Bryan, PhD
Well it's a burden on the family right? I mean you're putting your burden on your family whether it's Alzheimer's or whether it's stroke. You know you require 24 hour care many times on that. And so these are the things that we know scientifically everything we need to know about and how to mitigate it now, it's just getting this information into the hands of patients, into the hands of the physicians and practitioners who are seeing these patients that can lead them in the right direction. But I can tell you what I've learned over 25 years in academic medicine is that chronic diseases caused by two things and two things only. Your body is missing something that it needs or exposed to something it doesn't.

So if we replete missing nutrients in the body, the body heals itself, if there's something toxic in our body, whether it's a latent viral infection or you know, an asymptomatic dental infection or exposure to chemical toxic loans and we remove ourselves from the source of exposure and then give the body what it needs. Body heals itself. And that's how the human body is designed to work. And in that model there's no need or no room for drugs. Our body is never missing a synthetic compound that inhibits cholesterol production. Right? So that's never gonna make anybody, but our body is never missing something that's shuts down hydrochloric acid secretion from our parietal sins. So that's never gonna make anybody better remove your source from toxins. Move your source, move yourself from the source of toxins, good nutrition to make sure your repeated all the nutrients you need, it mobilizes our stem cells and improves nitric oxide production and we heal ourselves.

Michael Karlfeldt, ND, PhD
And also, I mean because people are thinking about mouthwash you know my my you know I don't want to have bad breath but if your digestion is functioning appropriately meaning that

you're able to digest your food appropriately you have the right kind of source of nutrients you eat cleaner. And then that in itself will reduce you know any kind of bad breath or anything like that. But then we have the nitric oxide is antimicrobial in itself. So you're actually by using mouthwash you're diminishing your ability to kill off pathogens that you don't need. And you are then killing off healthy healthy bacteria in your your mouth hole. Just like if you would take antibiotics to kill it off in the gut you're actually doing antibiotic in your mouth every day, killing off the healthy flora in the mouth.

Nathan S. Bryan, PhD

Now spot on and you make a very good point. There's a reason that we don't take an antibiotic every day for the rest of our lives because there's clear consequences of the negative health aspects of antibiotics. So obviously if you're sick and you have a bacterial infection there's a known regiment that kills these. But then you get all the G. I. Side effects from that diarrhea, the gastritis and all the bad things. So just so similar to not taking antibiotic every day for the rest of our life, we cannot use mouthwash to destroy the oral microbiome every day of our life. Yet many people are doing this once twice a day. So what we've discovered is that the greater the diversity in the oral microbiome, the healthier the ecology, the healthier the systemic health. But once you disrupt that ecology and decrease the diversity of the oral microbiome, bad things start to happen. So you get bad breath. The bad guys start outnumbering the good guys. You get periodontal disease gentrified us and that starts this whole vicious cycle. So if you allow this ecology to just create an environment that's conducive for good bacterial growth and diversity, then the good bacteria keep the bad guys at bay. You out analyze the oral cavity which then allows for the proliferation of the better bacteria because most pathogens are asset loving. When you drop the ph then it creates an environment for the bad guys to proliferate. So it's all about maintaining the proper ecology of the oral microbiome. And the number one thing you do to disrupt that is exposure to fluoride in your toothpaste and the use of an antiseptic mouthwash.

Michael Karlfeldt, ND, PhD

Yeah, that I mean that's such a huge message right there. I mean it's just huge. So you're mentioning then I mean because people will wonder, you know obviously do I have enough nitric oxide in my system. Where am I at? And what what are the appropriate measures, you know that that I need to take in order to be able to regain the amount of nitric oxide, just like you mentioned with with hormones, you check and see where my levels where my estrogen progesterone and we know that when they are low we just don't feel good and then we increase them and then all of a sudden we're happier. We have sex drive. You know, we feel stronger.

We're wanting to exercise, we wanted to be engaged socially. So everything just gets better. Life is just better. So it is it will would be a reason to be the same then with nitric oxide because hormones are signaling molecules and so is nitric oxide. You know, they tell the body what to do and so to how do we then measure? You mentioned that there is a simple test that you develop where you can then find out where you know where your level is at.

Nathan S. Bryan, PhD
Yeah, so this is an oral nitric oxide indicator test strips. So you just apply some saliva to the end of this test rip. Within a matter of three seconds it turns dark pink and that tells us your saliva is enriched and nitrite and you're able to reduce the nitrate from the bacteria. But you know I tell people it's a good tool to have in your toolbox, but it shouldn't be the only tool you're using because there's a number of false positives. There's no such thing as a false negative. So if you're low and you don't turn the test had pink and your low there is no such thing as a false negative. So we rely on symptoms. So I tell people if you have, if you have an elevation of blood pressure, your blood pressure is above, say 1 30/80 then your body is not making mycotoxin. If you're developing any degree of sexual dysfunction in men and women can't make mycotoxins. If you have hyperglycemia in type two diabetes, your body is not making mycotoxin.

If you have reduced blood flow and you're losing your memory and cognitive disorders, then your body is not making that up. If you get winded going up a flight of steps, then your body is not making a concept. So we rely on the symptomology, but also, you know, correlating that with the saliva test strip or even some functional vascular measurements. You know, there's something called pulse wave analysis and photography that you can get kind of, the structure and function of the blood vessels. That's really, you know, indicative of endothelial dysfunction. So there's really not a single thing that determines nitric oxide. We gotta look at the whole clinical picture and correlate symptomology with some biochemical readout on the test strip is a good indicator. But again, you have to be aware of the false positive.

Michael Karlfeldt, ND, PhD
And so let's say, I mean, if we deal with any of those symptoms, which obviously that's probably about 80% of any above, you know, anyone above 55 at least, you know, if not 90%. So if we deal with any one of those symptoms or if we would do, you know, use a little test strips and, and we can get that from your company. I would assume right?

Nathan S. Bryan, PhD
You can get them online. Now. You know, I developed these in 2010, they're readily available. I abandoned the patents on these test strips because it was some old chemistry, you know, that we thought maybe we would have some value in getting a patent on kind of a method of use. But to me, it was more important to have these test strips readily available than to, you know, have patents on them and have them limited from,

Michael Karlfeldt, ND, PhD
And it's something that measures nitrite, you know, in the saliva.

Nathan S. Bryan, PhD
That's right. That's a very important distinction. So nitric oxide is a gas and once it's produced in the body it's gone in less than a second. So we're not measuring nitric oxide gas, It's almost nearly impossible. And we can do it in the research lab. But clinically you can't do it. So we're measuring these metabolites of nitric oxide. And what's relevant in terms of this interior celebrates circuit is celebrating. I tried and that's what the test strips are measuring.

Michael Karlfeldt, ND, PhD
And so once you recognize that, you know, we are probably low, no matter what, we should still support ourselves, even if we think we're not low, even if we don't have symptoms, like we mentioned earlier symptoms comes quite a bit later and the person has been kind of in the process of developing disease for many years until symptoms show up. But let's say we have symptoms or we test and it's low, then we should then obviously we should get rid of mouthwash, we should make sure that we get off any kind of acid blockers. We should change our diet to more green leafy things, you know, so we can produce more of the nitric oxide from that. And then also then you have them certain gee that will then help to improve than the release is kind of like you're doing it for us.

So tell me a little bit how what you have is different because there's a lot of, you know, one of the products, you know, you talked about, L arginine is a common one, but then as we get older and we're not able to convert that to and nitric oxide, then L arginine is not as effective as it would be when we're younger. And then there are a lot of different beat products out there that talks about that. It supports the production of nitric oxide. So tell us a little bit about that landscape of what is good, what is not good? And what should we look at and what should we do?

Nathan S. Bryan, PhD

Yeah, that's a very good question. You know, consumers are confused because people in this space, everybody says the same thing. They can say the same thing, but yet there's very few products that actually generate mycotoxin. So as you mentioned, Argentine and Central Line based products are useless. I mean, to save your money, there's no need for that. Argentine and Central are produced through the urea cycle, your semi essential amino acids. So your body makes enough of these amino acids and dodges lee and from the breakdown of protein, whether explain proteins or animal proteins and so you don't need it. Furthermore, it could cause more harm than benefit. There's at least two studies now that date back to 2006 where if you give an Argentine to post infarct patients, these are people who just had a heart attack trying to restore their nitrous oxide. The Argentine actually led to a 50% higher mortality. So the Argentine killed more people than the placebo. And then the other was in peripheral artery disease, giving arginine to P. A. D. Patients. They actually got worse.

So again, if you try to shuttle nitric oxide through a dysfunctional enzyme, you generate super oxide instead of nitric oxide. You're exacerbating the condition. So argentine settling products 30 years ago, people thought they were effective nitric oxide products. They're not only ineffective, they can be dangerous. So avoid them at all costs. The other is, you know, beat products. I've tested hundreds of meat products on the market, 99% of them do nothing. It's really a deadbeat. In fact, we use these products as placebos in our clinical trials. So the beats work through their inorganic nitrate content. But again the body can only utilize this if it has the right oral bacteria. And with 200 million Americans using mouthwash, two out of three Americans wouldn't be able to convert the nitrate from their beads from their diet.

So what we've done is completely different. So we start with technology that generates nitric oxide. So in anything we do we kind of pre convert that nitrate so that we're not dependent upon the world microbiome because you know, you can't be a reputable company and put a product on the market only works in one out of three people. And what we do is we have product technology that works the same in every single person that ever takes. We can quantify it, we can verify it, it's objective. So we have the form of an orally disintegrating tablet. We've got a fermented beet powder. We've taken the Oxtail. It's to be pulled to be powder out of that. So it doesn't taste like beats. It doesn't look like beets. And so it's an incredible product technology that generates nitric oxide as soon as it's dissolved in water. So that's what we do. We create product technology that generates nitric oxide, gas that we can verify that we can quantify and it differentiates our technology from anything else on the market.

Michael Karlfeldt, ND, PhD
That's one. And yeah for all the listeners I use your product's gonna love them. So they're great products. So not not that you need my endorsement. I mean all your studies, everything is enough. So how do they complement each other? Because here you have the and it's N. O. To you. You know, it's the one and then the other one is called is like real beats or something like that.

Nathan S. Bryan, PhD
Eno beat.

Michael Karlfeldt, ND, PhD
Eno beats. Yeah. And so how do they, I mean do you need both or is if you take one then that's enough or I mean do they function differently?

Nathan S. Bryan, PhD
Well they function differently. You know the laws and the N. 02 U. Laws and is designed to be kind of like your daily vitamin C. Your daily vitamin D. Everything we do everything we're exposed to in the outside environment seems to disrupt micro oxide production. So these are meant to be a daily supplement supplement our mycotoxin one in the morning, one in the evening is typically sufficient. We developed the Eno beats product as a pre workout so people that can enhance exercise performance or just as an energy product, you know the market is saturated with things like the monster Energy. The Red Bull, the five hour energy that's really dangerous stimulant laced energy products that people take all the time. So we position this product is a natural energy source because we put makes nitric oxides were improving blood flow. We put electrolytes in there to improve cellular hydration.

So rather than dehydrating you like these energy drinks, we rehydrate you and then we put mitochondrial a teepee in there, which is cellular energy. So we want to position this so that people will stop drinking the very dangerous stimulant rich energy drinks and start getting a natural source of energy through the inner beats. And it actually improves their health rather than destroys their health. So they're completely different. And so for me, I take them, you know, I try to work out every day and go to the gym. So I wake up in the morning, take the lives and work out in the afternoon. So I'll take the beats right as I'm going to the gym and then at night um you know, sometimes I'll take a second lodge and other times just one loss today with the beet powder before workout. And that seems to work really well for me. You know, everybody's

different. The metabolic demands on each individual is different and so, you know, it's difficult if not impossible to prescribe a one size fits all. And that's the beauty of the clinician using your best medical judgment on recommending what, what may be best for individual patients, but it's clear that you need nitric oxide. And so I recommend, you know, certainly at the minimum one loss and once or twice a day.

Michael Karlfeldt, ND, PhD
And the loss and it needs to be dissolved in the mouth. I mean, kind of be chewed a little bit or

Nathan S. Bryan, PhD
We designed it to have a certain residents time. So a slow, deliberate dissolution rate. Because as this logic is dissolving, we're generating nitric oxide gas and we want that gas being liberated for as long as possible. So we designed it to dissolve within 5 to 6 minutes. So you just put it in your mouth, you move it around, don't chew it, don't park it under your tongue. It's kind of like a sweet tart. Just move it around. And as that matrix has fallen apart, we're generating in a gas That gas is absorbed. It's distributed systemically. We can see dilation of the blood vessels within about 12 seconds, putting it in your mouth. It's just a remarkable technology, nothing like it on the market well.

Michael Karlfeldt, ND, PhD
And Dr. Bryan, it's always a pleasure and an honor. And I'm so grateful that you are driving this vital information so that we can shift the type of care that we offer to people so that we can be more restorative preventive rather than reactionary. And then, you know, using pharmaceuticals has shut down normal physiological function that will then have a cascading effect more detrimental. You know, we need to shift the tide towards healthcare. True health care rather than sick care. So, thank you for playing such a huge role in that.

Nathan S. Bryan, PhD
Well, thank you and I appreciate you having me on, and it's an honor to know you

Michael Karlfeldt, ND, PhD
Thank you.