Introduction to Nitric Oxide and Dr. Bryan

– Welcome back to another episode of the reverse inflammation, summit body and mind longevity medicine. And I'm your host, Dr. Robert Lufkin in this episode, we get to explore the fascinating area of nitric oxide and its effects on longevity. And we're joined by one of the world's experts in the area. Dr. Nathan Bryan. Nathan, Welcome to the show. – Well, thanks so much for having me.

It's a great honor and pleasure to be with you. – Tell us a little bit about your background and how you came to be so interested in this fascinating area.

You know, just like any career, it's been a journey. I started out, you know, always interested in science and in medicine and did um you know, excelled that in high school. And then from there I went to the University of texas at Austin and got a degree in biochemistry and quickly realized that the job market for a bachelor's degree in biochemistry wasn't stellar.

So I realized in order to have a decent career I needed to go in further education and I took a 2 to 3 year kind of, not really a sabbatical but kind of kind of figure out what I wanted to do in life. And then in 1999 or maybe 2000 I enrolled at L.

S. U. School of Medicine in a PhD program in molecular and cellular physiology and it was there that I got introduced to the science of nitric oxide. It was a new field, a Nobel prize had just been award For the discovery of nitric oxide in 1998 and I was very fortunate to meet Louis Ignarro when I was a student there, we organized a conference and had him come in and give a lecture and kind of the journey to the Nobel Prize and had a chance to have dinner with him that night. And you know, as a naive student asked him a lot of naive questions. Uh it turned out they weren't that naive, they just weren't many answers to the questions that I asked.

And so for me it was a very rich source of uh you know, a chance to make a make a difference and to make contributions to science. I trained with a guy, a pharmacologist that had been the nitric oxide field for probably 20 years prior Martin Philish.

Dr. Bryan's Scientific Background

And then from there, you know, my role and really the, the work on my PhD was really an analytical chemistry because we had to develop sensitive and selective instrumentation or methods to produce or to measure nitric oxide at physiological levels, which is now animal or a symptom, a little concentration. And so once we figured that out, then we really had tools that no one else had in the field.

So, you know, as a student, I think I published six first author papers, I finished my PhD in a year and a half and then from there went and did a cardiology fellowship for postdoctoral fellowship at Boston University School of Medicine where I spent two years as a post doc and again publishing 12 papers a year.

And then I got recruited by Fred married, one of the other gentlemen that shared the Nobel Prize to join his team at the Institute of Molecular Medicine at University of Texas Health Science Center in Houston. And from there, you know, I was afforded a lot of the resources and just really intellectual freedom to ask any question that I wanted in the field. And we made a lot of discoveries.

I found a number of patents and I got several dozen issued patents in the field now. And it's really been a remarkable journey. But you know, it's really the being able to ask fundamental questions and then being able to design experiments to answer those questions is really one of the great aspects about being a basic scientist. – Before we dive into nitric oxide and and really explore that.

I like to ask our our guests uh maybe to set the stage by telling us what your view of longevity is. In other words, why do we age? There are many different theories and all our speakers seem to have a slightly different nuanced view of it. So maybe you could start off by just telling us the way you the way you look at aging and longevity. – Sure.

Well, you know, we're constantly wearing ourselves out right, we're in and the aging to me is just the inability to replace new cells that work properly. And so when you answer that, when you try to figure out what, when you answer the question, what does it take to make a new cell that works properly? Then you can really get to the fundamentals of longevity because we can't you know, we're exposed to so many toxicants in the environment and just daily activities that we have to replace and repair these old dysfunctional cells. And so aging to me is just the inability to replace these aging and dysfunctional cells. And so when we understand what that takes, then you can employ strategies to give the body what it needs to repair and replace dysfunctional cells. And then it's not just extending the quantity of life for the number of chronological chronological years.

But the quad because I think you and we would all agree that nobody wants to live to be 100 and 20 years old if we're not functional and we have to have somebody take care of.

– Absolutely! Yeah. Well now let's let's take a moment to start here and and clarify one thing, nitric oxide. There's another another word, another compound that sounds very similar to it that we want to immediately distinguish.

And that's nitrous oxide. So maybe just take a moment and and differentiate those. – Sure. You know, it's a common problem that people, when we talk about nitric oxide, they go, oh yeah, I love that.

I love nitrous oxide. Nitrous oxide is into oh it's a dental anesthetic. They're both gasses. They sound very similar but the physical chemistry is completely different.

So nitrous oxide is the dental and aesthetic that you get typically when you go to the dentist office called laughing gas. And that's not nitric oxide.

Nitric oxide is N. O. And it's a gas but it's a vaso dilator. So I like until people nitrous oxide will put you to sleep in nitric oxide is what allows you to function and have a sense of alertness and wellness.

– So what exactly is now nitric oxide then? – Well, as I mentioned, it's a gas but it's a gas that's produced in dodge city. It's naturally produced in almost every cell type.

You know. It was first discovered in our individual cells are actually first discovered in our immune cells. That's how the nitric oxide was first discovered.

But when it's produce it has many functions and its first function to be discovered was as a vaso dilator, meaning that once it's produced in the lining of the blood vessel that causes the smooth muscles surrounding the vessels to relax and dilate and that causes a normalization of blood pressure and it regulates blood flow to every organ tissue and cell in the body. Uh It's a neurotransmitter in the central nervous system, it's produced by our neurons and as I mentioned, it's it's it's a molecule made by our immune cells.

Macrophages, neutrophils monos sites and it's critically important in killing invading pathogens from viruses to bacteria. And really guys, you know, over the past 2.5 years, we really learned a lot about micro oxide in the immune response. Because we realized early on that the people that were getting sick and dying from covid were the people who couldn't make micro oxide.

These are older patients with high blood pressure, diabetes, previous heart attack african americans, Hispanics. So it makes sense because, you know, without getting too deep in the weeds, when you're expo exposed to a virus or a pathogen which we're exposed to every day, we live in a microbial world and some people get sick and some people don't.

So how do you explain the difference between people who get sick and who don't? And for instance, I'm probably

the best example. So when we're exposed to a pathogen, let's take covid, for example, it's a respiratory virus that attaches to the epithelial cells, the ace receptor. So when our body recognizes that it mobilizes our immune response, we go to the site of attachment and those immune cells generate a lot of nitric oxide, it shuts down the virus from replicating and propagating throughout the body so you don't get sick. So and people who can't make nitric oxide are mobilizing immune response, There's no defense mechanism.

Aging, Longevity, and Nitric Oxide

So the virus attaches it replicates propagates throughout the body and people get sick and unfortunately a lot of people died from it. So that's the importance of nitric oxide in a basic immune response in being able to mobilize a host defense.

– So so to recap the nitric oxide is a fundamental ubiquitous uh calm compound that's present virtually in every cell of our body. And it has these three really diverse but critically important functions of one endothelial ium and blood vessels and cardiovascular disease.

Everything associated with that and then to brain function and you know, conceivably all the neurodegenerative diseases associated with that. And then one more is immune function. And you know, as you mentioned, Covid and and everything else that the immune function does.

It's it's it's amazing. So I guess I don't know if I even need to ask this, but why is nitric oxide? So how is it related to longevity? And then we'll dive in a little bit there.

– Well, when you look at, so there's an age related decline in nitric oxide production. So if you look at and these are human studies looking at what's called industrial agonists.

If you infuse an agonist that would produce nitric oxide in the lining of the blood vessel. And then look at the results in Visa dilation. So there's about a 10 to 12% loss of what we call endothelial function per decade. You know, this starts, you know late teens, early twenties and a lot of this depend upon diet and lifestyle. But in general and population based studies if you look at the average, you know, by the time we're 40 years old, we only have about 50% of the nitro box that we had when we were younger.

And so now that the science is clear with I think over 100 and 85,000 scientific publications on nitric oxide, the science is really clear that it's the loss of production of nitric oxide. That's the earliest event, the onset progression of every major age related chronic disease.

And now, if you take that back to the question you ask of longevity, I think there's three main thoughts about longevity and the mechanisms of living longer.

So one is telomere shortening. So for your listeners, obviously the telomeres are the ends of the chromosome that with each cell division they get shorter. But you can control the shortening of the telomeres. So the science tells us that the shorter the telomeres, the shorter the life span. So if we can prevent telomere shortening or extend our telomeres and that's associated with longevity.

So that's one number two is loss of stem cell function. And so nitric oxide is the molecule that tells our own stem cells to mobilize and differentiate. So going back to this concept that presented earlier that if you if the stem cells don't get the signal to go and repair and replace tissue, then they don't and we age rapid.

And then the third one is mitochondrial function. You know, every age related chronic disease is characterized by mitochondrial dysfunction. So the mitochondria are the energy producing organelles of the cell and it's nitro cock that controls mitochondrial ATP production. It's nitric oxide that controls the number of mitochondria and how efficient they generate energy with oxygen.

So, you know, I presented this probably 10 years ago that nitric oxide is the unified theory of age because it controls the enzyme that prevents telomere shortening.

It controls stem cell mobilization differentiation and it controls mitochondrial biogenesis and mitochondrial function. So if you can't make nitric oxide, your telomeres get shorter, you lose stem cell function you develop.

And if you develop all three of those at the same time, then you're going to age rapidly and not have a very good quality of life. – Yeah. And you said that that that normally nitric oxide function decreases with age. And you mentioned 40 years old and all.

And I wonder in in longevity there's such a great interest in developing clocks to measure aging. You know, with the DNA methylation clocks or the chemical clocks. And basically people are making clocks of anything that changes reliably with aging. I wondered it seems like does nitric oxide decrease in a reliable manner. So that would be a reliable as as some sort of clock for aging as well? – Well, I think probably indirectly.

You know, it's very difficult to measure nitric oxide directly. So when we look at kind of the this age related decline in nitric oxide production. So that affects enzymatic production of nitric oxide.

Right? So the endothelial production of but about 20 years ago it was discovered that nitric oxide can be formed from certain components in our diet that overcome. And there are compensatory to loss of endothelial nitric oxide production. And now you can measure this through, you know, epigenetic changes in DNA methylation as kind of a biological clock.

You can look at vascular aging and look at vascular function measurements that are indirect measure of nitric oxide production. So when I talk about this age related decline of nitric oxide production, you know, that doesn't have to be the case.

You know, we now know that there are things you can do and strategies you can employ to prevent this age related decline in micro fox and that's what we've been focused on really for the past 20 or 25 years in my research lab and research program.

So we know, you know, again, I'm the best example, I think because I'm constantly measuring me and kind of what I do and how it affects, you know, our health and longevity and are really functional output.

So I was I just turned 49 on saturday, but I have a biological Of the 32 year old and we look at vascular measurement. So just because your chronological age doesn't have to match your biological, you know, to the contrary, I've seen 20, year old kids who have a biological age of a 60 year old.

To the contrary, you know, they're 60, 70 year old. People have a biological age of a 40 or 50 year old. So, you know, there are things you can do that will move the needle and change this biological clock depending upon what you're using as your clock and what you're in point in biological measures. – You're you're almost 50 and your chronological age, but your biological age is close to 30. Um, and that was with endothelial age.

Was that a DNA methylation or was that nitric oxide or imaging? Or what tests did you use for that? – There's a couple of things you can do. So I like to look at functional measurements, imaging.

Whether you're looking at crowded into the media thickness, that's one snapshot in time. Right. And I think that provides some some good information. But really the functional measurements for me and what we use is what's called venus seclusion photography.

Right? Or or you can look at the this non inclusive photography that looks at vascular structure and function. So their algorithms, there's FDA cleared medical devices out there that will give you your biological age based on the structure and function of your blood vessels and the ability of those blood vessels to produce micro toxin. That's what I've used.

I haven't used any of these other, you know, DNA methylation clock, you know, as you guys probably do you get pitched all the time on testing these and trying to, you know, incorporate them into but until they're really validated that for prognostic or diagnostic utility, then there's limitations and what they need.

– So many things affect nitric oxide. It sounds like nitric oxide levels in addition to to aging. Um What about stress or mental health? What what evidence is there for that affecting nitric oxide?

Nitric Oxide Deficiency and Health Symptoms

– Well, it's a two way street, you know, loss of nitric oxide causes, you know, mental disease, mental stress as well as and so and then once you develop that further produced suppresses nitric oxide production.

So it's this feed forward mechanism that if you lose the ability to produce nitric oxide, it causes decreased blood flow to certain regions of the brain develop neurological dysfunction, mild cognitive disorders. If not correct, advanced dementia. And Alzheimer's in stress.

You know, cortisol, the stress response actually shuts down nitric oxide not only decreases its activity and functional activity but also its expression.

So we have to do a better job of managing stress because that just, you know, mounts on and perpetuates this the symptoms of loss of nitric oxide production.

– And you mentioned um aging as as a primary driver for for lower levels of nitric oxide. What other things you mentioned, cortisol and stress, Are there other things like diet or lifestyle or other factors that can affect how our nitric oxide levels or causes to be deficient in them.

– Well, you know, it's it's the standard risk factors for cardiovascular disease. So smoking, sedentary lifestyle, high carbohydrate, kind of an unhealthy meal.

Um you know, obesity and even some pharmacological drugs, you know, we now know that an acid specifically proton pumping lead to an increase in a molecule called asymmetric dimethyl arginine or a D.

M. A. And that's been shown, you know, to lead to a 30 to 40% higher incidence of heart attack and stroke in people who have been on P. P. I. S for 3 to 5 years, that was worth.

I'm a good friend, john cook out of Houston Methodist. I think back in 2015. So if you if you shut down stomach acid production, you know, you shut down nitric oxide production and a lot of bad things start to happen. You lose acid base regulation you can't break down proteins into amino acids. So you get you know, food borne allergens and antibodies directed against certain peptide fragments.

We know that antacids are extremely bad and in fact because you know, they were never approved for chronic use. They were approved for acute use for chronic gastroesophageal reflux disease. But yet people are taking these every day for for many, many years sometimes the consequences are very clear.

So there are a number of and really any, everything we do, it appears to disrupt nitric oxide production. The american lifestyle, the american diet, you know, sedentary lifestyle, not sweating, the foods we everything contributes to loss of micro oxide production.

So it's really very tough and it's it's hard work staying healthy and preventing this loss of nitric oxide. – You mentioned the venus studies as an end epithelial marker for nitric oxide and all the the cardiac, the ct calcium scores one frequently used. And are they there are studies looking at either nitric oxide levels being related to that or are they help, can you help your calcium score with improving your nitric oxide or vice versa?

– Well, anecdotally, we've seen that in a number of physicians and cardiologists that have patients with an elevated coronary calcium score and then they'll, you know, utilize some of our strategies whether it's nitric oxide supplementation or just changing diet and lifestyle. And we've seen coronary calcium scores come down. But I think, you know, I'm not sure if there's a clear association between really a good prognostic value of coronary calcium.

Obviously a high coronary calcium is not good. But what we what we really focused on in terms of vascular biology is, you know, the the pliability of the plaque or the stability of the plaque because, you know, you can have as little as a 10% occlusion of the coronary arteries and have an unstable plaque and have an acute myocardial infarction.

Then there are people that have, you know, greater than 90% stenosis that have lived with that for many, many years and never have a cardiac event. So for me, it's not about the degree of of of the stenosis or the ACLU in the in the blood vessels. It's about the stability of the plaque.

And we know that if you can stabilize the plaque then people are you know, more resistant to acute M. I. And nitric oxide has been clearly shown the stabilized black, it prevents the inflammation, oxidative stress and immune dysfunction prevents platelets from sticking to the plot or to the the plaque.

So it's extremely cardio protective. But to answer your question, there's no randomized placebo controlled clinical trials on micro oxide affecting coronary calcium score that I'm aware of. – We've seen I guess now that aging is a risk factor for lower nitric oxide levels and then the american lifestyle which is more and more becoming the global lifestyle. So wherever you live, if you're even not in America, you're not off the hook.

Um So what are are there what are the signs that I might be deficient in nitric oxide? Are there are there specific signs that would would make us think nitric oxide or is it more generalized things?

– Well, you know that's a very good question. And people ask me all the time. Well how do I know if I'm nitro deficient and unfortunately, you know in the research lab we can measure, you know, plasma levels of nitric oxide metabolites or do biopsies and measure this but clinically it's not used. So unlike your cholesterol or vitamin D.

And you can't draw blood and say oh you're your numbers are bad. So we really have to rely on symptoms. And as you may imagine when you look at the effects of nitric oxide on human physiology, the symptoms are pretty broad.

So if you have an unsafe elevation in blood pressure, I mean you're not making nitric oxide that dilates the blood vessels and normalize blood in two out of three um have an unsafe elevation in blood. So that's one the first sign and symptom is really sexual dysfunction occurs in both men and women because if you can't regulate blood flow through the production of nitric oxide to dilate the blood vessels of the sex organs and you cannot get an erection whether it's in men or women.

So sexual dysfunction is what we call the canary in the coal mine. And it's really a sign and symptom of an underlying cardiovascular condition. And nitric oxide deficiency, diabetes. You know, insulin signaling requires nitric oxide. And if you can't generate nitric oxide in the cells then insulin doesn't get the sick. You don't get glucose uptake.

So insulin resistant diabetes is a sign of micro oxide deficient, mild cognitive disorders. If you can't remember where you left your keys. So when we recall memory we have to increase blood flow to the prefrontal cortex and you do that through the production of nitric oxide to profuse that region to recall memory.

So if you can make nitric oxide and develop mild cognitive disorders which are developing the vascular dementia and if not corrected. Uh huh. And then just loss of exercise capacity. If you get winded going up a flight of steps or walking, you know then that tells us that your body is not making nitric oxide, it can get, you know, these days inclusive crises or pain in the legs and peripheral disease the sign of nitric oxide deficiency. So really I think any major clinical symptom that's that we present with can be associated with nitric oxide.

It may not be causal but it's certainly an association with nitric oxide deficiencies. – And I've seen people talk about test strips for nitric oxide that they put in their saliva I think are those are those valuable at all or or – Yeah.

You know I was I developed that test strip back in 2010 because that was the first question people asked was how do I know if I need this? And so you know, really the only way to create engagement and kind of the first and only point of care, noninvasive diagnostic was to assess salivary nitrite concentration.

So I just use some really old chemistry called the grease reaction that we've used for many, many years in the research lab and applied that chemistry to the end of the test strip to where you can apply your saliva to that test strip and if it turns bright pink and that tells us that your body is able to re recycled? The nitric oxide production pathway through the centenario celebrates circuit. So I think there tell people they're a good tool to have in your toolbox but it shouldn't be the only tool you're using because there's no such thing as a false negative on this test. If you're negative you're negative.

Now then we have to kind of interrogate and figure out why are you nitric oxide deficient? But there are some false positive. So and the best example you know at a 50 year old overweight hypertensive diabetic patient with erectile dysfunction used that test strip and he turned it bright pink. Well obviously this guy is not replete in nitric oxide. He's obviously has all the clinical symptoms of nitric oxide deficiency. But he likes that test strip of bright P.

And so with further interrogation we found that he had an active oral infection. So the immune response in the oral cavity generates a lot of nitric oxide that shows up on the test strip. But systemically this guy is completely devoid of any nitric oxide production. So those are those are the kind of caveat.

So to answer your question, they're useful as a tool but again you have to be aware of some false politics. – Before we leave the oral cavity. I've seen on your website I think or in your podcast talking about certain mouthwashes to avoid.

Is that just because of the test strip they'll interfere with or is that systemically they will interfere with nitric oxide production. And maybe you could explain why how the mechanism is. – That's a great it's a great intro into this new pathway we discovered public 20 years ago. So independent of this nitric oxide that's being produced in the lining of the blood test, the neurons and our immune cells.

We generate nitric oxide from the diet from food. We'd so it's now realized that nitrate found primarily in green leafy vegetables can be reduced from metabolized by oral bacteria to nitrite And nitric oxide.

And humans do not have this enzyme. Humans do not have a functional nitrate reductase inside. So we're 100% dependent upon the bacteria, primarily oral bacteria that live in the crypts of the tongue.

These are faculty of anaerobic bacteria. We've been characterizing these now for more than 20 years. So what the science clearly tells us now is that if you disrupt this oral microbiome, you disrupt nitric oxide production from the diet.

So now what we found and I was on the doctor show I think last year where we we revealed that if you use mouthwash your blood pressure goes up and we were in a number of other groups publish them but you also lose the protective benefits of exercise.

So this told us that disrupting the oral microbiome is disrupting systemic nitric oxide production and the mechanism still isn't clear how how is nitric oxide being produced in the oral cavity affecting the second to second blood pressure regulation in the line.

So we're still, you know, trying to figure that out mechanism. We have a pretty good indication that is probably just inorganic nitrite or you know, that's bound to glutathione that's basil active that's produced through this pathway.

So the whole point is if you disrupt the oral microbiome you shut down nitric oxide production, your blood pressure goes up and you become nitric oxide deficient.

And now that creates a very interesting new kind of clinical readout because two out of three americans use mouthwash every day. I wake up in the morning switch mouthwash and I don't think it's that is two out of three americans that have an unsafe elevation in blood pressure. So we published on this, I believe in 2019 that if you eradicate the bacteria through daily mouthwash use in young, normal intensive healthy individuals, you can make them clinically hypertensive in seven days.

And then fortunately if you stop within four days of stopping mouthwash, you restore the diversity of the oral microbiome and restore nitric oxide production and you can see a normalization of blood pressure.

It's it's it's it's really any antiseptic mouthwash. So what we've used in these studies as cortex sitting. It's a prescription antiseptic that's used primarily for chronic halitosis and some, you know serious periodontal disease and gingivitis.

But you know, we've also done it with things like scope and Listerine, alcohol based mouthwash. And they all disrupt the oral microbiome and all disrupt micro oxide production. So tell people just like you have to get off an acid, you have to stop using mouth. – So, so there's really there's no labeling that would make the mouthwash safe because they're all basically antiseptic at some level.

– I mean when it when it's listed as an antiseptic, you know, there's kind of in this natural alternative world, there's a lot of people that are using essential oils or some so called natural rinses. And so you know, we just don't have any evidence whether they're disrupting that or not.

So we have to rely, I mean if it's antiseptic, it's antiseptic, it's killing the good bacteria is killing the bad bacteria, disrupting the diversity of the oral microbiome. And I tell people, you know, the same reason you don't take an antibiotic every day for the rest of your life is because of the known consequences disrupting the gut microbiome and getting systemic disease.

So it makes no sense to take an oral antiseptic disrupt the oral microbiome every day for the rest of your life. – I wonder if there are other things we that we consume orally that might have a similar effect.

How to Restore Nitric Oxide

I'm thinking like high alcohol concentration uh drinks, you know a liquor or something, you know could have that effect as well. – I don't think because you know, when we're sipping on liquor alcohol, we swallow it. Right?

So it does have a long residence time in the mouth. But here's the one thing that we have discovered, fluoride fluoride is an antiseptic. It's found in municipal water. It's found in most toothpaste.

Fluoride is an antiseptic and that's the reason they added to municipal water supply to kill any potentially infectious bacteria that may be found in the water supply.

So just like the fluoride in the water, the fluoride in the toothpaste acts as an antiseptic and it kills the oral microbiome. So tell people you have to get rid of fluoride in your toothpaste, fluoride is a neurotoxin. It kills your thyroid function that competes with the binding of the thyroid hormone with iodine.

Most people are deficient iodine, they're oversaturated with fluoride and its disrupts your thyroid function. – I guess we just lost crest as a sponsor for this program anyway. Um, yeah, so, so there's a there's a challenge here, like thinking about this were we all have decreasing nitric oxide levels with age and and probably with our lifestyle and our diet, maybe our mouthwash and our toothpaste too. Um, and then this the symptoms we have to test for it are fairly common that that most of us have. Anyway.

Um, so it and it sounds like then the best thing is to do things that will increase our nitric oxide levels, just assuming that they're they're low based on their age and everything else. So how do you regulate that when is enough and enough. And what maybe first start talking about what things we can do, Maybe diet supplements and even pharmacology drugs, medical prescription drugs. – Sure. So and that's a very common questions that people ask. Well how do I restore nitric oxide production and get my levels up to where they need. And you have to do two things.

It's very simple. Stop doing the things that disrupted and start doing the things that have been clinically proven to promote it. So we talked about what to stop doing. Get rid of mouthwash, get rid of floor. I get off in a message um And then so what's clinically proven to enhance nitric oxide? Well ma physical exercise, that's why exercise is

medicine because it stimulates nitric oxide production is probably one of the the simplest things you do. And americans aren't as active anymore.

You know the old saying and Cooper clinic has become a good friend of mine that Dr. Cooper, he says people don't stop exercising because they get old.

People get old because they stop exercise and I think there's a very important lesson to be learned there. We have to move, we have to stimulate nitric oxide production. Um you know sunlight there's certain wavelengths of life that frequency of energy stimulates nitric oxide production, releases nitric oxide that's found the metals releases nitric oxide that's found the Sistine tiles on proteins or even bluetooth ion. So there's both kind of wavelengths in the UV range as well as the near and far infrared or full spectrum infrared.

And then the other is um you know, diet, green leafy vegetables contain this molecule called inorganic nitrate, that the body can then convert into nitric oxide.

And you know, that's a challenge because we publish The paper in 2015 trying to figure out how much servings of vegetables like Broccoli or lettuce or kale or spinach would you need to eat in order to get enough nitrate to manage your blood pressure.

And there's regional differences in the amount of nitrate that's found in vegetables, you know, so it depends upon soul conditions, this whole field of agronomy.

So it's very difficult to determine if you're getting enough nitrate from the vegetables you're eating. So you know what we've done and kind of trying to provide solutions to every step in the pathway that becomes disruptive has developed technology that does it for you. And that's the basis for many of my discoveries and technologies that we wanted to, you know, in our drug discovery program with Dr. Murray at the Institute of Molecular Medicine.

The whole concept was if your body can't make nitric oxide that we have to do it for you. And then we now understand the Entomology, the biochemistry of the enzyme that we can restore the function of that enzyme and actually improve the body's own ability to make micro box and you know, that's I guess my claim to fame is that was the first person to develop a solid dose form of a nitric oxide gas. So we create this this lodge and this it's disintegrating tablet that when you put in your mouth and it's designed to have a resident time of about 5 to 6 minutes. But during that 5 to 6 minutes we're liberating about 30 to 40 parts per million in a gas. And in fact, that's the same amount they used clinically in the pediatric intensive care unit for premature babies born with pulmonary hypertension or even adults with pulmonary hypertension or during cardiopulmonary bypass surgery. So that's a clinically relevant dose of nitric oxide that's being produced in the oral cavity. It's vezo active.

You know, we can see dilation of the credit arteries within about 12 seconds of putting that laws into your mouth. That a number of studies showing that it can normalize blood pressure, improve exercise performance.

But also, you know, four hours after this. And we published on this in 2011 2012, we see about a 15% improvement in endothelial function. So meaning that we've re coupled the nitric oxide synthesis enzyme and now improved the body's endogenous production of micro cock side. And now we've taken that technology and we're developing FDA approved drugs using that same concept.

We've got a covid drug in phase Three clinical trials. We've got drug going into phase three clinical trials for ischemic heart disease alleviating the symptoms of exertion of angina. And then for this newer condition called ischemic non the coronary arteries. Which is a small vessel disease affecting women more so than men. But you know they develop signs and symptoms of ischemic heart disease. Were taken to the cath lab and angiogram reveals that there's no obstruction in the large vessels.

But the small vessels branching off the big vessels are clamped down and they become ischemic but it's non obstructive. So our nitric oxide opens up the small blood vessels and really has enormous clinical benefit for ischemic non obstructive coronary disease. – So this lozenge is available now.

And would you recommend taking that once a day and then it lasts at least four hours? – Yeah that's right. So we do. I mean I'm trained as a drug discovery chemistry biochemistry.

Right? So when we first discovered this natural product technology, when I was still a professor of medicine at the University of texas, you know we got a letter of opinion from some regulatory law firms on what do you need to bring this to market And since it was all natural product chemistry we really didn't need an I. N. D. Or an investigative new drug application to do this. So we brought this technology to market many years ago. And so it's available as an over the counter have since developed a second generation of these lozenges.

But really the whole concept of that is you take it, you know once or twice a day and it's as you know, as a physician it's very difficult if not impossible to describe a one size fits all. It's kind of a regimen.

So if you're young, healthy and pretty much in good health and we say one login today is sufficient. If you've got some challenges, then we recommend one laws and twice a day. That's really been shown to provide, you know the pharmacogenetics and kind of the the dynamics of this technology allows for 1000 twice a day to give you 24 hour coverage. – And then we so we talked about nutrition.

We've talked about some lifestyle and and these these powerful supplements. What about the prescription drugs that are available? You know, we've all heard of them, the Cialis, you know, the Viagra and the B. D. E five inhibitors I think.

Yeah what is this useful also for beyond erectile dysfunction but just restoring Eno levels for all the reasons you've mentioned. What what's your thought? – That it's a very good point.

So the PDE five inhibitors and those are drugs like Viagra Cialis and Levitra that are used that are approved for the treatment of male erectile dysfunction.

So there's a there's a misconception in medicine and even in the late public that these are nitric oxide donors These these drugs are not nitric oxide donors, they don't enhance nitric oxide production. What they do is they potentially eight nitric oxide signals. So nitro I tell people nitric oxide turns the switch on and these PDE five inhibitors keep this switch on for many hours.

And that's the reason people are warned against four hour erections, unsafe drop in blood pressure and all the side effect to come along with it. So nitric oxide binds to an enzyme without getting too deep into the science.

It creates a second messenger called cyclic GMP and its cyclic GMP. That's responsible for the smooth muscle relaxation. So this PDE five inhibitors prevent the breakdown of cyclic GMP.

So if your body can make a little bit of nitric oxide activates the second messenger then you potentially eight the Visa violation. That's the reason it works in erectile dysfunction. But we also know that 50% of the men that are prescribed these drugs for either E. D. Or for Bph urinary urinary symptoms of prostate hypertrophy don't respond. And the reason they don't respond to these medications is because there's not sufficient nitric oxide being produced in these patients to activate cyclic GMP. So there's no substrate for these drugs to work on. But here's what we've learned really over the past 10 years and people who have taken these drugs.

And I think so the point is if we can enhance nitric oxide production we can decrease the dose of these drugs and make them safer more effective. So I really like the once daily five mg Cialis. And and the reason for that is is that studies have shown now that people who were taken five mg, daily Cialis during Covid had a lower incidence of infection and severity of the disease.

Now there's clear evidence that people who have been on these drugs for many, many years decades have a lower incidence of alzheimer's and vascular dementia.

So there's something to be said about maintaining perfusion and circulation to every vascular bed, whether it's the vascular bed in the sex organs, with the vascular bed in the coronary arteries or the brain, you have to maintain

that circulation to get oxygen and nutrients to the individual cells.

So those are good. But again, there's limitations to those. But I think if you use them, you know, judiciously and you know, titrate down the dose, but really get to the root of the problem.

People are patient to prescribe PDE five inhibitors because their nitric oxide deficient. So I think my my objective is to train physicians and even patients.

So let's let's get to the root cause your root cause isn't an overactive pedestrians enzyme. Your root causes the nitric oxide deficiency. Let's address that.

Then there's no need for PG five inhibition theory. And I think there's another, there's a number of different mechanisms that can be exploited on that because in Western medicine, there's never this discussion by most physicians and how do we wean you off drugs. Right, let's come back and if this isn't working, I'm gonna put you on more. We're going back to this concept.

We started with that many of these drugs interfere with the body to heal itself. So the more drugs you're on, the less ability you have to repair and replace dysfunctional cells and tissues and your longevity is really compromised.

– Yeah, it's fascinating you mentioned the papers that are coming out showing the people on on the P. D. On the BD five inhibitor, the PDE five inhibitors um uh have decreased incidence of Alzheimer's disease.

And there's another one that came out with a longevity that they actually increased their longevity. And you know one would expect heart disease and everything else to be risky. And and it's it's interesting that the the clinical indication for the FDA, the approval was for blood flow to one particular organ.

– You know, we can't forget you know we can't forget that Pfizer started this drug program for patients was either in I believe it was pulmonary hypertension trying to dilate the blood vessels of the pulmonary circulation to alleviate pulmonary hypertension.

Which is still a poorly managed disease. And one of the side effects and common responses from the participants were better erectile function. So they abandoned the pulmonary hypertension and obviously exploited the market for erectile dysfunction. I think they've done very well with that.

– Yeah I I don't know if it's apocryphal or not. But I heard the story that in the clinical trials that the usually they're they're asked to return the drugs at the end of the trial, the unused drugs. But in this particular trial, patients were lose quote losing their drugs and abnormally high rate and they weren't returning them. Which right.

Exactly, exactly. The this is this has been a this has been a great talk here. I wanna be respectful of your of your time here. One quick question about cell repair, I think you touched on it before.

Maybe you just revisit nitric oxide specifically as far as repair for longevity. You could just revisit that briefly. – Yeah. This really came on the radar in 1996 when it was discovered that, you know when you lose nitric oxide.

And this I believe the study was done in the most efficient mice, we can genetically delete the nitric oxide producing enzyme. And it was found that these these animals have less viable stem cells.

Whether they're the uh you know, pluripotent stem cells that are mobilized. And then several studies later. And and we even with Dr. Murad discovered that if we can if we stimulate nitric oxide production early in the differentiation process, we can target certain stem cells to go to cardiac beating cardiac minus sides.

So there's different stages and differentiation where nitric oxide comes into play, but if you can't make nitric oxide then not only do the residents stem cells not get the signal to mobilize, they don't differentiate.

PDE5 Inhibitors and Clinical Uses

So then, you know, when people getting a lot of stem cell injections, you know, early on there were Tara Thomas and a lot of adverse events from that.

So again, if you if your body doesn't have what it needs to get the signal to repair and replace. Then even giving stem cell exogenous stem cell therapy isn't going to fix the problem, we have to and our whole process is what we're trying to recapitulate physiology or restorative physiology.

And that's the basis for our drug discovery. We're not we're not developing pharmacology were developing restorative physiology, but I think on a broader level, you know what I've learned in 20 years of science is that chronic disease, whether it's Alzheimer's diabetes, autoimmune disease or cardiovascular diseases caused by two things and two things. Only the body is missing something that it needs for its exposed to something that it doesn't.

And so in that paradigm there's really no room for drug therapy because, you know, going back to uh you know, early days in the early 1900 forties, um you know, most chronic diseases are caused from a nutrient deficiency.

We know that most americans, 95% of americans are deficient. I don 75% of americans are deficient magnesium and these are critical co factors for enzymatic reactions and then the other is the body is exposed to something that doesn't need, whether it's mold mycotoxins, environmental toxins, uh latent viral infections, uh something from the environment. So if we replete the missing nutrients and eliminate the toxins in the body, body heals itself were regenerative beings.

We just got to get out of the way and stop doing the things that disrupt. – Yeah, that's such a good point that for most of the chronic diseases we face at least the ones associated with aging pills and surgery may treat the symptoms but they don't really change the underlying course of the disease. That's that's so important.

Well, we've talked a lot about nitric oxide. I wonder um aside from aside from the nitric oxide space, which is so exciting, what are the other areas, anything else in longevity that you're most interested and the most excited about? – You know, it's a very good question.

But you know, I live in my own little microcosm of nitric oxide. And so what I try to do is and I think that's one of the reasons we were successful in basic science because as you guys know, basic scientists are, you know, you're always taught to go from bench to bedside take your discoveries into the clinic. But that's like fitting a square peg in a round hole, right? Cause everybody has their favorite molecule but it may not be clinically relevant.

So what I did and that was the beauty of working at the Texas medical center was you get to collaborate with a lot of really talented physicians. So we take really complex clinical observations, Bring them back to the lab, model them in the lab and then go back to the clinic.

So really what works is bedside to bench back to bed side, you have to model the disease, understand the ideology disease and now you're not fitting a square peg into a round hole. So now what I like to do is take physicians who have complex cases and then let's figure out how does nitric oxide play a role in the ideology of the disease. And then start Employing simple clinical strategies that these gives physicians new tools to use in their armament.

But so I you know, obviously I pay attention to the literature and other things that are relevant. You know, I wasn't at all interested in immunology until obviously all of us were forced to become interested in immunology in 2019 or 2020.

Stem Cells, Repair, and Closing Thoughts

But now it's it's it's fascinating because now we have a clear understanding of nitric oxide role in respiratory viral infection which otherwise would have probably been that impetus for understanding that.

– Before we go, maybe you could tell our audience the best way for them to reach you or follow you on social media or your website. – Well, I send everybody to my educational website, I'm not here to sell you anything but really just provide some objective education.

And so that's DrNathanSBryan.com. I have a six minute video on there that'll tell you kind of show you how nitric oxide works biochemically. Come on instagram, Dr. Nathan S. Bryan, I'm on twitter at Doctor nitric and then obviously we live in a world where people are searchable. So you can search me online most of it's still good I think. – Well, great, well thank you so much Nathan for spending time with with us today in this session and and thanks again for all the all the great work you're doing in this in this really interesting space.

– Well, thank you very much. It's a pleasure to be with you Robert and Stephen and thanks for the invite and I look forward to to continue this discussion helping us educate the world on nitric oxide.

And for those that you know, I've published several books, I've got a new book coming out this year called The Secret of nitric oxide. And uh so that will be really really, it's it's two fold.

It's a personal journey. Kind of my journey from Discovery and basic science to really to create awareness around nitric oxide. Published several textbooks. But my latest book called functional nitric oxide nutrition is an easy lay read. I'll give this is a free gift to your listeners an e copy of that but really provides that. It's a 90 minute read.

That'll give you kind of an in depth understanding of nitric oxide and really how you can employ some strategies in your own life to restore your nitric oxide.