



DR. ROBYN BENSON + SELF CARE REVOLUTION PRESENTS  
**HEALTHY TRAVELER'S GLOBAL SUMMIT**  
SPEAKER TRANSCRIPT

**Dr. Robyn Benson:** Hello everyone! Welcome to the Healthy Traveler's Global Summit. My name is Robyn Benson. I'm a doctor of oriental medicine and the founder of Santa Fe Soul Center for Optimal Health. Into the past 23 years, I have loved helping my patients solve their most critical challenging health concerns. And this summit... the creation of this summit happens to come from treating so many of my patients who travel on a regular basis, pilots and flight attendants. But also I've traveled to 70 countries and I can always just say I've learned some of the most amazing health tools from some of the indigenous people in the world, and some from... some of the nurses and doctors that I've trained with. And it's such a pleasure today to continue this journey, The Healthy Traveler's Global Summit with Dr. Nathan Bryan. As we crafted this whole summit, we wanted to come up with speakers to certainly talk about food, and talk about water and talk about the ways that we can travel internationally in a safe way. And also, we really looked at some of the scientists who are... have some amazing research to share with you when we think about how we work on this higher level. And that's why when I found out about Dr. Bryan's work... quite a few years ago, actually, I've seen him speak several times; I thought this is absolutely pertinent that you all will learn about nitric oxide today from one of the world's leading... I'd say researchers in nitric oxide. So, Dr. Bryan thanks for being here today. How are you?

**Dr. Nathan Bryan:** I'm doing well, thanks. Robyn thanks for having me over.

**Dr. Robyn Benson:** I'm glad you're here all the way from Aspen on vacation with your family.

**Dr. Nathan Bryan:** Yes. Coincidentally, we're doing a healthy traveler's summit and I'm right in the middle of a vacation, a skiing trip here in Aspen, Colorado.

**Dr. Robyn Benson:** Well, this is fantastic. So, I'm going to tell you a little bit about Dr. Bryan and then he... we just thought would be the best way for all of you to really understand how critically important it is to increase your... and optimize your nitric oxide levels by sharing a PowerPoint and it's... It's fantastic; it's the one that I've seen before. So, I'll come back and we'll have some questions as... towards the end of it, just to give you an idea of how this particular interview will go. Alright, so Dr. Bryan earned his undergraduate Bachelors of Science degree in Biochemistry from the University of Texas at Austin and his doctoral degree from Louisiana

State University School of Medicine in Street Port, where he was the recipient of the Dean's award for Excellence in Research. He pursued his post-doctoral training as a... Christine fellow at Boston University School of Medicine and the Whittaker Cardiovascular Institute. Dr. Bryan has been involve in nitric oxide research for the past the past 15 years and has made many seminal discoveries in the field. These discoveries and findings have transformed diagnosis and treatment of many chronic diseases associated with nitric oxide insufficiency. Dr. Bryan is also an entrepreneur and author who has successfully commercialized several of his discoveries. He has four issued US patents and six pending worldwide. Dr. Bryan is the founder of Chief Science Officer of Neo-genesis labs, a Texas-based company started to commercialize nitric oxide-based technologies in diagnostics. And as you listen closely, you will completely understand why we wanted to include this amazing presentation in the Healthy Traveler's Global Summit and why you are going to want to go out and get something to eat, a NEO40. Okay. So, again thank you for being here and we'll just turn it over to you.

Dr. Nathan Bryan: All right. Well, thanks Robyn. So as you'd mentioned I've been involved in the nitric oxide field for about 15 years. In fact, they got started a year after the Nobel Prize was awarded for the discovery of nitric oxide. So... we knew it was an important molecule, we knew there was a lot to be learned. And so for me as a basic scientist, it will do an exciting field and exciting time to be involved in nitric oxide. So throughout my training in fellowship, we had seminal discoveries that I think transformed the way we thought about how the body generates and produces nitric oxide. What goes wrong in people who become nitric oxide deficient? And then we started to implement strategies that could restore or replete nitric oxide in humans. And then I was recruited by Ferid Murad, one of the gentlemen who shared the Nobel Prize in 1998 to join the faculty at the University of Texas Medical School of Houston, where I was a fourth number of years... about nine years, really throughout to drive discovery program. So as you may imagined in Academic Medicine we're involved in drug discovery. So, through that process we were able to discover symmetric product chemistry that generated authentic nitric oxide gas. So that was kind of the basis of our discoveries in technologies and innovations that lead to the portalization of the NEO40 Technology. So it's been... it's been quite a ride, it's been very gratifying because we hear every day from patients and consumers who take the NEO40 and immediately get that. It was some serious health challenges that otherwise, they weren't able to address. I think now, perhaps, if you'd like to go into the powerful... [Cross-talk 00:05:21.19]

Dr. Robyn Benson: Can I ask you a question?

Dr. Nathan Bryan: Yes, of course.

Dr. Robyn Benson: Can you just tell our... all of our listeners how you got into medicine in the first place and how this all happened?

Dr. Nathan Bryan: Well, I was always interested in science even as a high school student. And then I was a bio-chemistry major at University of Texas at Austin. I was involved in undergraduate research there and was really intrigued by this concept of... really the intellectual freedom that you're afforded by science. So when you learn basic scientific methods, you're really allowed to ask any biological question, any question you want and then design experiments to answer those questions. So as a kid, I was always been curious, that really fascinated me. I thought there was a number of important questions in science and medicine that haven't been addressed. And so utilizing what we learned through the training, it's... that caught my attention and really picked my interest. So it's really... and I don't... the scientific method, they were taught, the training, I don't have to subscribe to that. I don't think it works. I'm more curiosity-driven rather than hypothesis-driven. And so that really goes against the way we were trained in the so-called scientific method.

Dr. Robyn Benson: That's great. So you... just before we get started with the PowerPoint. You travel a ton, don't you? You're a jet setter. You're in New York, you're in Colorado, you're all over the place, and internationally too.

Dr. Nathan Bryan: Yes, I've travelled 60 to 80,000 air miles every year, drive another 30-40,000 miles all across the state of Texas when it's probably easier to drive than fly. So I'm very familiar with the challenges of travels, especially international travel. And it's exhausting but there are simple techniques and I'm hoping to learn a lot more from watching the Healthy Traveler's Summit to help my own health and well-being as we travel.

Dr. Robyn Benson: Awesome. The speakers are incredible. So I just want to say Dr. Turner, one of our amazing speakers. He happened to say when we interviewed him. He said, "Do you have some... someone talk about nitric oxide? It's really critical to this traveler's message." And I said, "Absolutely, we have Dr. Nathan Bryan." And he said, "You know what? That man should win the Nobel Prize award in science." So I just wanted you to know that. He holds you in such high regard. And so, just to all of you listening, we're very fortunate to have Dr. Bryan with us today. So, thank you. So we... now we'll get started with that PowerPoint? Okay.

Dr. Nathan Bryan: So how's that, Robyn? Can you [Cross-talk 00:08:08.25]?

Dr. Robyn Benson: There we go. Got it! Awesome.

Dr. Nathan Bryan: Okay, so what I'd like to do is spend the next maybe 20 minutes talking about how to upgrade your nitric oxide levels to ensure healthy travel every day. And so, now when I turned professor at a major college of medicine, but obviously the reason we're on here is to discuss this molecule, nitric oxide. It's a very simple molecule in nature. It's one nitrogen, one oxygen. It's recognized as one of the most important molecules produced within the human body. And we're about 30 years after the discovery of nitric oxide and 135... probably 140,000 papers published in the scientific and medical literature tell us that nitric oxide plays a role in virtually every biological function that's responsible for maintaining normal blood pressure, normal circulation in the cardio-vascular system. It's critically important for regenerative medicine, nitric oxide is what tells our stem cells to mobilize and differentiate and repair tissue. It's a neuro-transmitter in the central nervous system. It's how our cells regulate proliferation of apoptosis and programs so that.

And through, the main molecule in the neuro-general tract is responsible for normal natural function. So you can begin to imagine when you lose the ability to make nitric oxide, there are a lot of things that go wrong in the human body. So it's not just a cardio-vascular problem. It's already the onset of Alzheimer's and type 2 diabetes, and sexual dysfunction and immunocompromised reactions. And so, in 1998, a Nobel assembly in Stockholm awarded a Nobel Prize in physiology of medicine to Bob Furchgott, Louis Ignarro, and Ferid Murad. Because they have realized how important the discovery of this was, specifically concerning nitric oxide as a signaling molecule in the cardio-vascular system, so by way of history, it was Ferid Murad who discovered... and this was in 1977, the late 70s. The drugs like nitroglycerin or organic nitrates that have been used for 150 years prior to the 70s work through the release of nitric oxide. Now, prior to Fred's discovery was... physicians used nitroglycerin for the treatment of acute angina because it worked but they didn't know how it worked or why it worked. So that was an important discovery in its own right but really, it amplified Ferid's discovery when Bob Furchgott discovered that our endothelial cells, and I'll show you a schematic of that here shortly, released the substance that causes blood vessels to dilate.

And so Bob and his 1980 nature paper didn't know what this was but he turned it endothelium derived relaxing factor, EDRF. So this was a huge discovery in the field of astrobiology, but no one knew what EDRF was. And then, in 1987, seven years later, it was Louis Ignarro, along with Salvador Moncada, they've discovered EDRF is nitric oxide. So now the pieces of the puzzle were put together because nitric oxide either released through a medicine like nitroglycerin or nitric oxide donor, or nitric oxide is generated in the endothelial cells in our blood vessels,

cause blood vessels to dilate, relax, and you can increase blood flow profusion, oxygen entry delivery to downstream tissue. So that's, I think still, one of the fundamental discoveries in the history of cardio-vascular medicine and it was Ferid who brought me to... recruit me to join the faculty in the University of Texas and he has been a great good colleague and he's written a foreword of two of my textbooks over the past seven or eight years. And really, to highlight really what I just said, it's really that... that's what Ralph Folster said in 1998, the day that the Nobel Prize was awarded. This was the front page of the New York Times, the discovery of nitric oxide and its function is one of the most important in the history of cardio-vascular medicine.

I think that that [Inaudible 00:12:10.17] still holds true today. But I think it's important for people to understand how nitric oxide works and what it is and I think that can be illustrated in this little schematic here. But these are endothelial cells. Endothelial cells are the single layer of cells that line all the blood vessels in the body. In fact all blood vessels and all lymphatics. And so these cells were thought for number of years just to be kind of a barrier between the blood vessel and how the inside of the body or extra cellular space, but when you activate these endothelial cells, either through sheer stress or some agonist, it tells this enzyme in the endothelial cells, nitric oxide synthase to make nitric oxide. So nitric oxide is a gas, perhaps I failed to mention that. But what it produced... it diffuses in three dimensions. So part of it can diffuse into the lumina, the blood vessel where it interacts with platelets and monocytes and neutrophils cells, keeps blood cells from sticking to the lining of the blood vessels. The part of it diffuses then its underlying smooth muscle and it activates an enzyme called guanylate cyclase. And this was an enzyme that Ferid Murad had worked on and discovered that becomes activated when you generate nitric oxide. And then this enzyme converts GTP the site of GMP, I don't want to get too technical with this.

But what I want to do is illustrate that this is a very important pathway because PD5 inhibitors are fast-filled illustrated in [Inaudible 00:13:39.06] work through inhibiting the breakdown of the second messenger cycle of the GMP. So there's two fundamental principles here that we can begin to understand vascular biology. And number one is that if the endothelial cells can't make nitric oxide, there's no signal to turn on the cycle of GMP production. So 50% of the men in which Viagra is prescribed seen no effect because they can't make enough nitric oxide to turn the signal on. So there's no sub-straight distance to work on. So that's an important clinical observation. But perhaps more importantly is it really corroborates the basic science behind this because the problem with erectile dysfunction, or endothelial dysfunction for that matter, is insufficient nitric

oxide production in the vascular endothelial? So my research over the past 15 years has been geared toward how do we restore normal nitric oxide production in these endothelial cells because once you do that, everything else will take care of itself. And perhaps, there'd be no need for these types of drugs because the self-threatening pathway of cascade will be intact and can work. And this is just a schematic showing that if you... even if you have people with advanced coronary disease or had a heart attack or stroke, obviously, they have a clot that's built up in their arteries, they become nitric oxide deficient.

But if you deliver a drug like nitroglycerin that releases nitric oxide and it can still dilate the blood vessels, and that's the reason you get a most immediate response from acute angina. You could complete symptomatic relief within a matter of seconds or minutes when you give a drug... when you give the nitric oxide donating drug. This is the busy slide and I don't expect all the readers to read thoroughly... your audience to do this. But the point of this, really, is to convince the people that watch this because it's not me telling you that nitric oxide's important. It's what the 130,000 published papers on nitric oxide tell us that it's important. In fact, the loss of nitric oxide production is recognized as one of the earliest advance in the onset progression of all chronic disease, probably the cardio-vascular disease and the number one killer of men and women worldwide. But interestingly, it's not only associated with all major cardio-vascular risk factors that it has predictive value for future Atherosclerotic disease progressions. So being able to diagnose and monitor nitric oxide production before patients start developing symptoms or disease is critically important. And I think as we get through this, it's extremely important for people who travel because when we set sedentary for a number of hours and we're exposed to different altitudes in travel, all of these have shut down nitric oxide productions. And unfortunately, this is... there's an age dependent loss of nitric oxide production.

So we'd lose about 10 to 12% of our nitric oxide per decade so by the time we're 40 or 50 years old, we only have about 50% of the nitric oxide we had when we were young and healthy. And this is really the basis for age-related disease. So loss of nitric oxide is the earliest event in the onset progression of this age-related disease. So our thought process was if we can prevent the age-related decline of nitric oxide production, can we prevent age-related disease? Anything from hypertension, Alzheimer's, type 2 diabetes, all of these have a clear association with insufficient nitric oxide production. And so that's kind of what we set out on and so... I think it's important to... if you develop an inability to generate nitric oxide and you become NO insufficient, what are the clinical symptoms or manifestation of NO insufficiency? Well, it's not

surprising that if you lose the production, the ability to produce the molecule that maintains normal blood pressure, then you can develop high blood pressure. In fact, that is the case. The nitric oxides also involved in mitochondrial ATP production. That's really how our cells generate energy. So nitric oxide controls the efficiency of mitochondrial ATP generation, it controls the number of mitochondrial.

So, fatigue, people get lethargic and fatigued and unable to exercise because they can't make nitric oxide. Atherosclerosis, the vein from those of which is a huge issue in travelers who are sedentary for a number of hours in an airplane or in a car. Alzheimer's is now a clear association with reduced blood flow to the prefrontal cortex and vascular dimension, even Alzheimer's, erectile dysfunctions both in men and women is what's considered a [cameo 00:18:16.14] and coma and it's probably one of the earliest advance or signs of NO insufficiency. Pyrophoric disease, immune dysfunction, uncontrolled cell-proliferation and chronic inflammation. You can see as we go back to that, one of the first slides that because nitric oxide's involved in all these biological functions, that it's not just the one clinical presentation of nitric oxide insufficiency. Patients present different signs and symptoms. But all of these are related to insufficient nitric oxide production.

Dr. Robyn Benson: I just want to mention, Dr. Bryan. In my book, the Healthy Traveler's Guide, I mentioned like five or almost all of those, actually. The certain... the entire lambrosis issues is really huge, the hypertension, fatigue, and immune dysfunction, all so common. And so this is just a great solution for everyone listening, knowing that this is badly important if you want to travel healthy on a regular basis. So for pilots and flight attendants who are in the air all the time, and people who are frequent flyers but also, the people who are over 50 that tend to have more of a predisposition to some of these conditions. This is why that whole idea of self-care and good food, I know you're going to get into that. All of that really matters so that you don't end up with any of these. So...

Dr. Nathan Bryan: Yes. Absolutely. So and people, if they would never put the pieces of the puzzle together that, this is a... such a simple problem and is insufficiency of nitric oxide because all of these signs and symptoms may seem unrelated to standard medical care.

Dr. Robyn Benson: Right.

Dr. Nathan Bryan: So the ultimate question that we ask years ago is if this is so... such an important molecule, then how does the body control and regulate nitric oxide production. And then what goes wrong with these pathways that lead to the onset development of all these symptoms and diseases. And

this is very complex but I think it's important for the people to understand how nitric oxide is produced in the human body. So for years, people thought "well, I'll just give it L-arginine because L-arginine is substrate, the precursor to nitric oxide. And if I can remember, the L-arginine products out there that lead them to market for a number of years. Now here's the problem. So if you have a normal, healthy and endothelium, then this enzyme, nitric oxide synthase can convert arginine into nitric oxide or we can get sertraline by product. That's illustrated here. But what people failed to understand was this is probably one of the most complex and complicated reactions in the human body. It's a five electron oxidation so you're basically taking this, what's called the guanidino nitrogen or arginine and converting it into nitric oxide.

But the problem is that if the enzyme is uncoupled due to a number of factors, then it can't convert arginine into nitric oxide. And in fact, that's the problem in people who are nitric oxide deficient. It's not that they're deficient in L-arginine, they're deficient in the enzymatic machinery that converts arginine to nitric oxide. So the analogy I'd like to you use, if you get a person who is nitric oxide deficient and has endothelial dysfunction, giving them an L-arginine and/or L-arginine type product is like putting gas in a car with a blown up engine. See, it's not going to get you where you need to go because we have to fix the engine. And so the human... this single human disease now where there's a deficiency of L-arginine. So giving L-arginine to a patient whose nitric oxide deficient doesn't make sense biochemically. In fact, there's a couple of studies that show that if you give high dose of L-arginine to post-MI patients or patients with pyrophoric disease, they actually get worse. And so it's not L-arginine and it's not recommended to patients that have vascular issues. And so, the issue now is in the re-acclimating step is oxidation of tetra hydro biocrine. So understanding that if you get to provide all these co-factors and the substrates to recouple nitric oxide synthase, then and only then can you get a conversion of arginine to nitric oxide.

So that's the enzymatic... the enzymology of this reaction. But what's nice... so let's assume you make nitric oxide, has a half-life of less than one second. So our focus has been where does nitric oxide go and what does it become? Well, we now know that NO combine to glutathione can basically, extend the biological half-life from one second half to tens of minutes and they transport it as nitrosative glutathione at that. Nitric oxide reacts with oxygen in cells and tissue to form nitrite or oxyhemoglobin and form nitrate. And we now know that this can be recycled back through... oral commensal bacteria. So this really gives us two final strategies to restore nitric oxide production. One is through diet; nitric containing green, leafy vegetables to beet juice. And the other is through fixing the



vascular endothelial nitric oxide synthase enzyme. And so that's been our... kind of modus operandi. It's how do we fix both of these pathways to restore normal nitric oxide production?

So I've kind of touched on this but in the... understanding how the body generates nitric oxide leaves us with really finite strategies to enhance and restore nitric oxide. You could use L-arginine, ascorbic acid, folic acid or tetra hydro biocide. But as I mentioned, this require functional nitric oxide synthase enzyme. And the problem in people with endothelial dysfunction and NO with deficiency is this enzyme doesn't work typically and so.... These types of strategies have limitations. There are also not independent sources of NO; all molecular weight and nitroso bio, nitrite, nitrate, nitro fatty acids, organic nitrates and there has been some strategies employed by big formative develop hybrid drugs but large adhesives have been really unsuccessful in getting to the market. If I want to take you through... kind of this whole molecular mechanism of vascular disease and plaque buildup and atherosclerosis. Because it's recognized that the earliest signs of atherosclerosis or what we call vascular inflammation. And inflammation is characterized by monocytes and neutrophils and all these blood cells that struck, sticking to the lining of the blood vessel. And over time, they'll actually migrate through, they'll be modified by your own immune system, develop these stone cells and this... over time, this is what develops plaque in the lumina of the blood vessel.

And over time, this plaque becomes unstable, it ruptures and it's typically the end of the road for a lot of patients because they suffer of fatal heart attack or debilitating stroke, depending on a lot of traumas ends up. But it's also recognized that if you can prevent the early adhesion or sticking of these blood cells to the vascular endothelium then it can prevent this whole vascular atherosclerosis process. So I'll show you some video, and providing my positive paper we published probably seven or eight years ago now. But there's mouth models that you can induce atherosclerosis and you basically feed them a western diet, then we can quantify in real time. So these are monocytes and neutrophils. So you can see they're stuck to the lining of the blood vessels, the blood vessels begin to look like Velcro. Everything sticks. You could see there's almost a traffic jam here. So there's... beginning stenosis of this artery. And so we can quantify this, you can assess the score and... Inflammatory score by the number of monocytes that stick and then actually immigrate through the vascular endothelium. But if you get that same atherogenic diet and you have nitric oxide on board and you fix the problems. You can say that the blood vessels actually more dilated, the monocytes and neutrophils home

along the vascular endothelium looking for sides of the artery but they don't stick.

So you can completely suppress the vascular inflammation response to a poor diet by generating nitric oxide. So one of the earliest events in the onset and progression of vascular disease. So, we talk about food and exercise... diet and exercise really being the answers to preventative medicine, especially travelling. It's really difficult for people who travel to eat the right amount of food and to certainly exercise. But I highlight this because your ability to generate nitric oxide actually predicts how well of an athlete you are, how well you can perform athletically. So this is a paper published by some friends and colleagues in Germany showing that your ability to generate nitric oxide is... predicts how well you can exercise. So these are young healthy, moderately trained athletes. The problem is, if you get older patients, you begin to let them exercise, they don't generate nitric oxide, they can't generate nitric oxide so they're unable to exercise. In fact, this is the mechanism for the exercise stress test, the patients who have coronary disease. So if your coronary arteries can't generate nitric oxide to dilate your coronary arteries to deliver more oxygen to the working heart muscle, then they can't sustain that exercise regimen fulfill the exercise stress test and typically, they'll take them out to and gone the CAT lab and put a stand-in or worst case scenario, they have by-pass surgery because they have completed inclusion of the coronary arteries. So again, I think the highlight, the importance of exercise and diet are really critical to restoring nitric oxide production and preventing this age-related decline in nitric oxide production.

Another interesting study that were published several years ago with the group that have case Western was looking at people that live at high altitude. Especially coming from sea level in Austin Texas to here in Aspen where about 9,500 feet at base. And so the oxygen tension is much... is lower so we're breathing less oxygen in for inspiration. So most people develop high altitude sickness or acute mountain sickness. The people that live in Tibet, which is 12,000 feet above sea level at the base of these mountains, they don't develop altitude sickness. So these anthropologists were interested in understanding the mechanism of how these Tibetans adapt to living in high altitude. This is the paper we published in the proceedings in National Academy of Sciences in 2007. And really, what they have done in setting this event for a number of years was showing that even though they're breathing in less oxygen per breath, they actually deliver more oxygen per unit time than people living at sea level. So the question is, obviously, this is a vascular response but they're delivering more oxygen although they're breathing less oxygen per breath. And so the question was in how we got involved was could this be

a nitric oxide related phenomena? And of course, I'm certain the answer is yes for I wouldn't be showing this. But this just shows that Tibetans have about 50 to 100 times more nitric oxide bio they availability than in people living at sea level. So they adapt to high altitude because they adapt and start generating more nitric oxide.

So here's the critical component, you can actually mimic this in people that live at sea level. So if you go... this has been known for a number of years because people thought it was just generating more blood cells and I think that's part of the response. But if you take athletes and send them up to 3 to 4,000 feet and they train, you see a step-wise increase in nitric oxide production, provided they're healthy athletes with the normal healthy endothelium. But people that have endothelial dysfunction and nitric oxide deficient, they can't make nitric oxide. They'll never acclimate and adapt by generating more nitric oxide because they can't. That's the reason people develop altitude sickness when they travel overseas or even from... for instance like we did, Texas up to the Rocky Mountains for vacations. And so, I'll take you to just a couple of a clinical trials. Here's the technology we've developed. Again, four issued patents, five publicity clinical trials, but this is NEO40, it's the only disintegrating tablet. So when you put this lozenge into your mouth, we designed it to have a certain resonance time of about 4 to 6 minutes. And it has that lozenges dissolving. It's generating authentic nitric oxide gas. In fact, about 25 to 30 parts per million gas. It's the only technology in the world that generates authentic nitric oxide gas. So that... we set out to do two things, one if you could develop a nitric oxide therapy, you have to give a rescue dose of nitric oxide because these people have been deficient for a number of years, they can't make nitric oxide so we have to do it for them.

So as that lozenges is dissolving, it's generating about 25-30 parts per million NO gas which is the same amount that you would give in the neonatal intensive care unit with premature babies or poorer hypertension. So it's a nitric oxide donating technology. We receive P-plasma concentrations within about 20 minutes of a crowd that was just published in the Journal of Clinical Hypertension by Dr. Mark Houston in Nashville, showed that if you took hypertensive patients and gave them a single NEO40 lozenge in about 20 minutes, he saw a statistically significant reduction in those systolic and diastolic blood pressure. And 60 minutes later there was a further reduction in blood pressure. And so that's really what we think of the acute effects of nitric oxide and probably some of the effects of the nitric oxide that's generated by the lozenge in the wall cavity. But four hours after a lozenge, and understanding, going back to that schematic I've told you where the enzyme becomes dysfunctional, and we can now recouple that nitric oxide synthase

enzyme, and really enhanced vascular production of nitric oxide. We... there's a device called the endopath that you can measure endothelial nitric oxide production. And four hours later, after a single lozenge, we see about a 15% improvement in endothelial production. So, really showing that this lozenge does two things. One, it generates authentic nitric oxide gas that no other technology in the world does, we see dilation of blood vessels, you see reduction in blood pressure. All the things that you would expect nitric oxide to do.

But four hours later, long after that nitric oxide is gone, we see an improvement in the endothelial indigenous production of nitric oxide. This is a schematic of carotid arteries, so the carotid arteries are what go up to your neck and feed the brain. So you can get an internal diameter of this blood vessel by ultrasound, and then 10 minutes after the lozenge, you see about a 13% increase in blood vessel diameter. In understanding the laws of hemodynamics, this translates into a 34% increase in blood flow. So 10 minutes after you take the NEO40 lozenge, we're perfusing the brain by improvement of about 34%. And here's some cool imagery we can use to... demographic imaging that really shows heat radiation so we can indirectly measure perfusion and this is just one example of a 49-year old female that's a chronic smoker with Raynaud's syndrome. Raynaud's is a micro-vascular disease characterized by cold hands, cold feet and it's because the micro circulation doesn't work, it can't make nitric oxide so you never get perfusion of the digits. And so 10 minutes after lozenge, you can see that the digits start to improve and people get complete symptomatic relief within a matter of minutes, only take the NEO40 lozenge. So, I didn't have time... honestly don't have time to go to all five published clinical trials but I think we could summarize the effects of all these clinical trials by this slide here.

So we think we have a superior nitric oxide technology because we provide authentic nitric oxide gas. So if the patient can't make nitric oxide, we do it for you. And for years, people thought that nitric oxide was a ...full of calorimetric kind of pyramid mediator. Meaning nitric oxide can only act in the cell in which it was produced, or a neighboring cell. But in 2007, we published a medi-paper with the proceedings of National Academy of Science showed it... it was actually an indifferent function of nitric oxide. So nitric oxide can act almost like a hormone. It can be produced in one tissue and have an effect in a distal tissue. So when we generate nitric oxide in the oral cavity, it's affecting the biochemistry and physiology of our tissues in the heart, the liver, the kidneys, because of that indifferent function of nitric oxide. And there's no other technology in the world who does that. But probably, most importantly, as we promote endothelial production of NO, so we fix the enzyme that becomes

dysfunctional in patients that are nitric oxide deficient. And I think it's important that if we live by these principles of basic physiology that if we give the body the nutrients it needs, the bodies are remarkable organism and the fact that it can regenerate and repair. But we have to give the body the nutrients it needs or technologies off. [Cross-talk 00:35:11.19]

Dr. Robyn Benson: We have a question here. Can you elaborate a little bit more about what's causing that enzymatic deficiency? So I'm just curious about... obviously the toxic world in which we live. And specially, jet fuels and certain... things that we're breathing in the air on a regular basis. That's going to be affecting this too, right?

Dr. Nathan Bryan: Yes, absolutely. So it's just like anything else. It's multi-factoral. There's not a single event that leads to the uncoupling or dysfunction of the nitric oxide synthase enzyme. So there's some genetic issues where people have some snips or... that cause them insufficient or a breakdown of that enzyme. But really, its diet related. When people don't eat the right foods, it'd be oxidized tetrahydrobiopterin and cause the enzyme to become uncoupled. So there are number of things. But you're right, I mean we're under assault every day, all day from environmental exposure to toxicants, to poor lifestyle. Really, sedentary lifestyle is that they... and poor diet are responsible for the majority of people with endothelial dysfunction because you can activate nitric oxide production by moderate physical exercise. But if people aren't getting moderate physical exercise, they're sedentary, they never activate. This nitric oxide synthase enzyme becomes dysfunctional. I think it's relevant in the travel world because as you've just mentioned, we're exposed to all of these toxicants and we're sitting sedentary, for instance on trans-continental flights, we're sedentary for eight, 10, 12 hours. I don't know about you but a lot of the airline food that we eat in the airports and even in flight aren't really designed... they're not what we call high in nitric oxide index.

Dr. Robyn Benson: Right.

Dr. Nathan Bryan: So we've have... in some of the basis for our technology is... look, people aren't going to eat the right amount of foods and they're not going to get the right amount of physical exercise and it's really a compliance issue. We know we're supposed to eat the right foods and the right diet and get physical exercise but the issue is people don't for a number of reasons. One, they're too busy, they're travelling or they just... are like not to. They'd rather eat these junk foods, snack foods and play video games which is probably the worst thing you can do in terms of enhancing nitric oxide production. So that was... those are all the considerations that we have when we generate this technology is... okay, understanding that and people can't make nitric oxide then we have to do it for them.

Dr. Robyn Benson: How about GMO foods? Jeffrey Smith is one of our speakers also. He's a... around the globe and he speaks to many audiences about how GMO foods are impacting our body. So I'm just curious if there's been research done.

Dr. Nathan Bryan: Well, people... and I always said people have to understand the reason why you're genetically modifying food. And it's to make them resistant to the herbicides and to... that they're...

Dr. Robyn Benson: Right.

Dr. Nathan Bryan: So I don't think there's an issue with the genetic makeup or the new proteins that these plants or vegetables are expressing, it's the herbicides that they're exposed to and that we ingest when we eat GMO foods. The reason people genetically modify food and then the fact that the plant or the taste... that it really allows them to put herbicides on them and then we eat these, we're exposed too. So a lot of these will shut down nitric oxide production. So what they consider the people... at least be aware of genetically modified foods is that the toxins that we're getting by ingesting these are certainly affecting... inhibiting nitric oxide production.

Dr. Robyn Benson: Excellent. Thank you.

Dr. Nathan Bryan: So there's no tolerance, as I mentioned, this plant-based natural product chemistry we use on non-GMO ingredients in both our meat products and our NEO40, we see drug-like effects without the side-effects, the clear product experience that's now being demonstrated in five published clinical trials, we have four more clinical trials underway now, four issued patents, six pending worldwide. But I think it's important also to know who Neogenis Labs is because a good technology by the company that's not based on credibility and integrity, then...do not take it to... stop doing the world any good. But we're a five year old Texas-based company, with season experienced executive leadership, our CEOs are former president of Dell computers, the University of Texas, and his students own my patents, its faculty there for all those years, we have designed our patent rights over at U.T. But we fund this company, Neogenis Labs and now we have the exclusive license to commercialize my technology.

And the University of Texas is an equity partner in Neogenis Labs. In fact, we're now one of the most successful U.T. portfolio companies in the history of U.T. Science Center. But we're dedicated to science delivering quality safe and effective product solutions. And so our metric is always, we won't bring the market any technology that's not proven by basic science, as well as clinical trials to demonstrate safety and ethic. And so, I'll just conclude, and then you and I can chat on some things that we

have missed because as I said, we can't... didn't have time to tell you everything. But I think, hopefully, I've convinced people that their profound effects of NO on health and disease, recognizing NO insufficiency is critical for prevention of disease, lifestyle modification, taking... implementing strategies or supplements like the NEO40's fundamentally improve health moving, especially the travelers, safe and effective nitric oxide supplements can have profound effect on the health and disease, and most importantly, I think all nitric oxide products are not created equal. Educate... it's important for people to educate themselves to differentiate between efficacy and creative marketing. Because we've been successful in the marketplace, we've had other companies that have come and try to mimic and copy our technology and they've been largely unsuccessful with that because they don't know how to quantify nitric oxide.

In fact, we use a lot of products out there as our placebo in our clinical trials because there are so-called the based products or nitric oxide products but they have no clinical efficacy. And so with that, I will just... I think that's the last slide. But I'll give you a couple of references too because there's... to educate yourself, there's a couple of references and obviously, I'm an author on two of these books so I understand my conflict of interest here. But I think the purpose of a lot through need those books is to take the complex science of nitric oxide in this particular work, put it in the easy to understand life version. So this is the nitric oxide solution. It's available through Amazon or from our own website. But this is one of a more technical read that's well-referenced, this is a book I edited with Joe Macaluso whose chair of medicine in Harvard Medical School and chief of cardiology at the Brigham and Women's in Boston. Spring of Humana asked us several years ago to edit this work because it was such an important piece in the nutrition series. And this is... we're working on the second edition of this now. But this is really... kind of the... probably the most comprehensive published work on nitric oxide, particularly nitrite and nitrate, that's out there now. So this has been a fun project working with Dr. Macaluso and really inviting the world's experts in each subject matter from diet and nutrition to epidemiology, to cancer, to cardiology, cardio-vascular health, all that's included in this particular book here. So with that, I'll open it up back and see if I can stop sharing and get back on screen.

Dr. Robyn Benson: There you are. That was great.

Dr. Nathan Bryan: Good.

Dr. Robyn Benson: Really helpful overview. So there's a number... isn't there a number that we have for all the Healthy Traveler's Summit people?

Dr. Nathan Bryan: Yes, there is. In fact, we will get that. But of course there is and we'll get that so people can have access to that information and away from the office, we come in... I've been out of communication but we'll certainly get that ahead to be done...

Dr. Robyn Benson: That will be great and I'll certainly put that in my book because I think that it's really important to know that this is really digestible. I... we use this in my clinic and more and more now. In fact, I have a 45-year-old patient with E.D. And he's never been able to solve this issue. So he's already seeing a reaction by taking the NEO40. So let me just talk a little bit about that. Is it something that people can use in...? Obviously, can use instead of Viagra? Was it... and probably safer?

Dr. Nathan Bryan: Well, here's what we... our state of response is they should always consult their physician before they start any subterranean drug. So here's what we know that people that have erectile dysfunction in both men and women are typically because they can't make nitric oxide. And so the lozenge that we've generated and brought to market generates nitric oxide. Both the [caring 00:44:02.29] and restores the indigenous production of NO. So here's what we see clinically, we don't have any published clinical trials on E.D., we're in the process of designing those and starting those now. But people who don't respond to PD5 inhibitors like Viagra or Cialis Levitra will then begin to supplement with nitric oxide with the NEO40, these drugs then begin to work. So there's really two critical issues, I think, that are important in terms of E.D. And you've got to understand that a lot of people can't tolerate these PD5 inhibitors because of the side effects. So the challenge is always; can you lower the dose to where they won't have that... we can mitigate the side effects, and the best example of this is the once the daily Cialis so patients typically respond better to that because they don't have the side effects. But the challenge is they still don't get the effect that they're happy with. So the satisfaction of that is agreed.

But they can't increase the dose because they can't tolerate the side effects. So here's what we're seeing and we're now designing a drug to demonstrate this clinically is that if you include the NEO40 with a lot of those PD5 inhibitor, then that response is actually enhanced. So people who aren't satisfied with the PD5 inhibitors now take the NEO40 and they see the super charge affect and they're satisfied with their... the quality of their erections and the frequency. And so, people seem very happy with it and so... we generate nitric oxide and nitric oxide does a lot of things including improving erectile dysfunction.

Dr. Robyn Benson: So you mentioned beets and dark green vegetables, what are other some really excellent foods with... that will help with this nitric oxide deficiency?



Dr. Nathan Bryan: Yes. It's a good point. I didn't have time to go...

Dr. Robyn Benson: Yes.

Dr. Nathan Bryan: Yes. So probably 10-12 years ago, it was recognized that there are certain foods... we published a paper now that showing the dietary approach is to stop hypertension, the diet that's actually endorsed by the American Heart Association, works because of certain foods and vegetables that are high in nitrate. And so we've quantified out probably 400 different foods and herbs and traditional medicines to look at there in what we call the nitric oxide index. Now here's what stands out; kale, spinach, arugula, beets, so not even green leafy vegetables that have been known for decades to be cardio-protective, have anti-cancer properties. But then here's the other issue, Robyn, and people failed to understand is that all these known created in a fact, we just got a paper published several weeks ago, showing that if we took samples of vegetables at retail from Raleigh, New York, Dallas, Chicago and Los Angeles, and for example, if you eat spinach in Los Angeles as opposed to Chicago, there's as much as a 500 full difference in the nitric oxide or nitrate content with that vegetable. So all vegetables are created equal, it's the growth conditions, the sole conditions, the time of harvesting and the sunlight, all that controls the nutrient density of these.

So, you mentioned beets and beets have been on the radar map for a number of years because it was recognized in the 2012 Olympic Games and a lot of the athletes were drinking beet juice to enhance their nitric oxide activity. But... and so now people are starting to put beetroot extract in their products calling it the nitric oxide products. But we find that there's as much as a 500 full difference in the nitric oxide activity of beets or raw kale or spinach or a lot of these things that people are now putting in nitric oxide products, but has no nitric oxide activity, whatsoever. So, they... and it's just naive and these people don't know the nitric oxide field may say that beets are... can enhance nitric oxide so they put it on their label. To me, it's just window dressing, it has no biological activity, whatsoever. In fact... [Inaudible 00:47:42.29] test we tested.

Dr. Robyn Benson: So a lot of these great green powders and red powders in the market might not be doing what they say they are, is what you're saying?

Dr. Nathan Bryan: Well, I'm not saying that. In terms of nitric oxide, they may not be doing. So there's obviously other health and nature... [Cross-talk 00:47:59.04]

Dr. Robyn Benson: Right, right.

Dr. Nathan Bryan: But it's... we know how to quantify and measure nitric oxide but typically, no one in the company does or change it. So yes, to your point that the greens products or the red products that are saying that they can help promote nitric oxide production, some do but the majority of them don't because of the quality of the ingredients that they put in their products. And they're not... they never... our metric is always, has been and always will be nitric oxide. So before we put an ingredient in any product, we measure the inherent nitric oxide activity and how that body can actually convert it into nitric oxide. So that's the difference between our technology and other competitive products out there.

Dr. Robyn Benson: Just one final question about this epidemic of diabetes, and obesity, especially among the younger population. So we're just... this is just another indication of what we're going to see more and more of... chronic disease with so many of these young kids that are obese right now and have diabetes.

Dr. Nathan Bryan: Yes. It's still not surprising it's a lifestyle disease. It's a poor diet, not enough physical exercise. In fact, you can overcome diabetes by changing your diet and getting more of physical exercise. But here's what we've known... we've known for years that people with diabetes... type two diabetes have a higher incidents of cardio-vascular disease because diabetes itself causes reduction in nitric oxide production. But now, there's convincing evidence that nitric oxide deficiency actually causes type 2 diabetes. So there's a number of evidence to support that. So if you knock out the nitric oxide's same place genes in mice, they develop type 2 diabetes, showing that loss of hydro peroxide is causal for type 2 diabetes. And we've been able to understand the insulin pathway to the extent that we can now restore normal insulin signaling through the NEO40 or enhancing nitric oxide production.

[Cross-talk 00:49:52.19]

Dr. Nathan Bryan: So we can really see that in type 2 diabetes, they take the NEO40, we've seen improvement in fasting glucose levels, we see them improve the vascular function. But diabetes is one of these... again, multi-factoral diseases that... but the good thing is that it's completely modifiable by diet and lifestyle

Dr. Robyn Benson: Wow. Well so, for every traveler, that's listening... how important this is to consider this. This is a really important solution, especially when I think about any pilot that would want to be taking this NEO40. But for all of you, just recreation travelers, I know I travel at time. I'm starting to take this on a regular basis because I just feel the effects of travel on lots of levels. So that's why we wanted to bring you here. This has been fantastic. And also

for the brain function, right? For all of us, we get that brain fogged with travel, increase your nitric oxide levels will certainly help that... the circulation with your brain.

Dr. Nathan Bryan: Yes. I think it's important. So when we talk about performance enhancing, it's not just athletic performance but it's middle acuity and all these things that we're faced with when we travel. The good thing about the NEO40 is it can restore nitric oxide and generate nitric oxide. But I think for travelers, the convenience of that is just unmatched. It's allows... that you can put in your shirt... shirt pocket and just pop it... I pop it before we take off...

Dr. Robyn Benson: And it take the... I'll say that I love the taste of the NEO40.

Dr. Nathan Bryan: Yes. That was... consumers are going to take this, it has to taste well. So it's a citrus berry flavored and we have no complaints over the past five years in terms of the taste. So again, a very safe, very efficacious, great tasting, convenient product.

Dr. Robyn Benson: Awesome. Well, thank you so much for joining us today and sharing your great message and for all the people that have never known about the nitric oxide, you are going to know for the rest of your life that this is the best way to age well, it's one of the most important ways to ensure healthy travel on a regular basis. So wonderful. Really appreciate you.

[Cross-talk 00:51:49.28]

Dr. Robyn Benson: Okay. Take care.

Dr. Nathan Bryan: Thank you so much. Goodbye.