

Rip Esselstyn:

Hey everybody, I hope you're doing well. I want you to know that I'm coming along with my broken foot. The stitches came out on Tuesday. I started swimming again. I feel like I've really gotten over the hump with this broken foot. I'm going to have to be on crutches or on a little stroller for another month, as I'm keeping weight off it, but things are looking good. This episode is going to be a doozy. If you're getting ready to pop an antacid or take a swig of your favorite mouthwash, wait, hold up just a moment with me. Here's why.

Rip Esselstyn:

If you listen to last week's episode of the Plant-Strong Podcast with my father, you know he is a fanatic about boosting your nitric oxide in order to basically bump up the production of your healthy endothelial cells. Why? What exactly is this miracle molecule? It may be new to you, but know this, our body's ability to produce nitric oxide is paramount to staving off killers like stroke, heart disease, and other vascular complications like, men, erectile dysfunction.

Rip Esselstyn:

Today, I take a deep dive on the subject of nitric oxide with the preeminent expert on the subject and the author of the Nitric Oxide Solution, Dr. Nathan Bryan. My father has found his work and I knew that I had to have him on the show to open your eyes and mine on what seems like a very complex topic. Fortunately, we break it down into interesting and actionable takeaways for you. What is nitric oxide? No, it's not the laughing gas that you get at the dentist's office. What happens to our body's ability to create nitric oxide, and why does it diminish as we age? What foods can we eat to pump up the production of this magic molecule? Why do so many common over-the-counter products like mouthwash, and acids, and antibiotics crush our body's ability to produce nitric oxide?

Rip Esselstyn:

Dr. Nathan Bryan says, "Chronic diseases is caused by two things and two things only. One, the body missing something that it needs; or two, it's exposed to something that it doesn't need." Today, we want to give you what your body needs. So, listen in closely and say Y-E-S, yes to NO, nitric oxide.

Rip Esselstyn:

Side note here, the initial interview took place at my office in February prior to COVID-19. Since then, there has been a tremendous amount of research into the subject of nitric oxide in preventing and treating the Coronavirus, especially in the African American population who, as the data show, are the most vulnerable. You'll want to stick around for the quick bonus segment at the end as I caught up with Dr. Nathan Bryan just last week via Zoom. Enjoy.

Rip Esselstyn:

If you want to learn more about the wonders of nitric oxide and all things plant-based, I invite you to join us for upcoming Plant-Stock 2020 Weekend, where my father will be giving his paramount lecture on preventing and reversing heart disease. This online learning weekend is packed with science and practical application. It's a chance for the whole household to learn together. Visit [plantstock2020.com](http://plantstock2020.com) today to learn more.

Rip Esselstyn:

All right, I am here with Dr. Nathan Bryan. Nathan and I... We actually got to know each other or have got to know each other a little bit because one of your business partners, a man named Bill Hough reached out to me because he really wanted to get in touch with my father, who, as I'm sure you know, is a huge fan of nitric oxide. So, I basically brokered the phone call, made it happen. While I was listening to the conversation that you were having with my father, I was like, "Holy smokes. I've got to get this guy on the Planet-Strong Podcast because he is probably the foremost authority on the planet and nitric oxide and everything about nitric oxide," which my father refers to as the magic molecule. I think you refer to it as the magic molecule.

Rip Esselstyn:

It seems like most Americans don't know what it is, what it does, how important it is to disease prevention. So, I'd love to spend the next 30 minutes or so with you talking about what you've discovered since plunging yourself into the study of nitric oxide, and how our listeners at home can benefit from this knowledge, what they can do to increase their nitric oxide production, make sure that they're not somehow disrupting the NO production, and things of that nature. So, for starters, what is nitric oxide?

Nathan Bryan, PhD:

Yeah, it's a very good question. It's recognized in the scientific and medical community as one of the most important molecules produced in humans. So, it's a gas that has a half-life of less than one second, but it's produced in the lining of the blood vessels, where it regulates blood flow and oxygen delivery and is responsible for maintaining normal blood pressure. It's a neurotransmitter in the central nervous system. It's how our immune system fights off invading pathogens.

Nathan Bryan, PhD:

So, when you lose the ability to make this critical magic molecule, a lot of things go wrong. So, your blood pressure goes up. You lose the regulation of blood flow. You develop erectile dysfunction, vascular dysfunction. You develop cognitive disorders. The neurotransmitter function in the central nervous system is paused, and then you become somewhat immunocompromised because your immune system can't generate nitric oxide to fight off some pathogens, whether it's bacteria, viruses, or fungal infections. That's kind of the basis of what nitric oxide is and does.

Rip Esselstyn:

So, what I mean if this is considered one of the most important medical discoveries in the last 100 years, why is it that if we were to go... Let's say, we went down to Whole Foods Market, right? We asked 100 people, "Do you know what nitric oxide is?" I bet you 90 would say, "I have no idea. Are you talking about the laughing gas at the dentist?" They don't know. I mean, why do you think that is?

Nathan Bryan, PhD:

Well, historically, we know that it takes on average 17 years for new discoveries to become so called standard of care or made aware to the public.

Rip Esselstyn:

Interesting.

Nathan Bryan, PhD:

We're about 20 years after the Nobel Prize was awarded and probably 30 years after the discovery of nitric oxide. So, even that is a little bit slow based on the average. I think the reason that is, is that clinicians don't use this as part of their initial screening. There's no labs that you can go. You can't go to your physician and say, "Hey, Doc, what are my nitric oxide levels?" They can tell you your vitamin D levels, your cholesterol, all that, but there's no commercial labs that will tell you what your nitric oxide levels are. So, that's number one.

Nathan Bryan, PhD:

And then number two, there's really no nitric oxide-based therapies on the market that even if they did diagnose nitric oxide deficiency, there's really nothing on the market in form of drug therapy that corrects this. So, one thing I've learned is the physicians don't like to diagnose something they can't treat it. Number two, that really we've been slow in developing drug therapies that correct nitric oxide deficiency.

Rip Esselstyn:

Now, is there a way of if I want to go down and figure out a way to measure the nitric oxide that I have coursing throughout my body, is there a test or something I can do?

Nathan Bryan, PhD:

Yeah, that was a question that we were faced with over 10 years ago when we developed a nitric oxide technology we brought to market. That was the number one question, how do I know if I need this? There was really no standard lab. So, I developed a salivary test strip. So, this is a colorimetric semi-quantitative test that you just supply your saliva to the end of this test strip. Is some old chemistry that if it turns dark pink, you know that your body's making sufficient nitric oxide? If it doesn't turn colors, then it tells us that your body's nitric oxide deficient. So, that's kind of a quick point of care.

Rip Esselstyn:

Is it pretty accurate?

Nathan Bryan, PhD:

It is pretty accurate. So, if you don't turn that strip pink, then your body is nitric oxide deficient. There is no false negative. But what it doesn't tell us is why your body's nitric oxide deficient? But then we can start to interrogate these different pathways and figure out exactly what's going on in your body and then take the steps to correct them. But there are some false positives. So, for instance and we see this quite often, a patient is clinically sick. They have high blood pressure. They have erectile dysfunction. They have diabetes. They're just sick, but yet they spit on the test strip and turns dark pink. Well, that tells us then that the clinical symptoms actually outweigh the biochemical test.

Nathan Bryan, PhD:

What we're finding is that these patients who show all the hallmark clinical symptoms of nitric oxide deficiency, but the test strip is dark pink, that they probably get an active oral infection. It may be symptomatic or asymptomatic, because there's a local activation of the immune system that's generating a lot of nitric oxide either on the gingival tissue where there's gingivitis, periodontitis, or they've got an active infection. So, that's a local immune response. It's not really reflecting systemic bioavailability.

Rip Esselstyn:

So, you talked about in one of your several books about how as we age, our nitric oxide production typically decreases. Why is that?

Nathan Bryan, PhD:

Well, there's two ways the body makes nitric oxide. These are discoveries over the past probably 20, 25 years. The first pathway is through an enzyme that's found in the lining of the blood vessels. So, that enzyme is called nitric oxide synthase. It's found in endothelial cells, and that's really the age-related production mechanism that declines the older we get. So, we know that usually we lose about 10 to 12% of that 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 younger. So, that's bonafide, verified scientific data and there are a number of things. That's on average, I should say.

Nathan Bryan, PhD:

But we now know that as these new diagnostic or medical devices come to market that tell us our vascular age, we're now seeing 18 to 20-year-old kids with a vascular age of a 50 or 60-year-old. Then to the contrary, we're seeing 50 or 60-year-old people with a vascular age have a 20 or 30-year-old. You don't want to follow the average because the average person in America... I'm not interested in being average. The average person is overweight, sick, broke, and unable to exercise or perform to their full potential. So, we have to figure out how do we get away from or deviate from that average?

Nathan Bryan, PhD:

So, the standard cardiovascular risk factors, smoking decreases nitric oxide production, eating an inflammatory diet, processed foods, things like that cause endothelial dysfunction. So, all those standard cardiovascular risk factors lead to a decrease in nitric oxide production, sedentary lifestyle. So, that's the pathway that gets less and less with age. But this backup redundant pathway that we can use through diet, primarily through the plant-based diet. Green leafy vegetables that are enriched in inorganic nitrate. We've recognized a pathway in humans that can utilize the nitrate to serially reduce it down to nitric oxide. S

Nathan Bryan, PhD:

So, plant-based diet is important. It's good, provides benefit, but there are a number of steps in that pathway that are required for patients to get the benefit of a plant-based diet. I would say, a nitric oxide benefit of a plant-based diet.

Rip Esselstyn:

You're saying there's a number of steps that are required when you're eating, let's just say Plant-Strong, a lot of green leafies, you're a huge fan of, right?

Nathan Bryan, PhD:

I am.

Rip Esselstyn:

What are some of those steps so that our listeners can maximize those steps?

Nathan Bryan, PhD:

We're learning many caveats to this. So, number one, we've quantified the amount of nitrate in green leafy vegetables, both conventionally grown and organically grown. We published this I think in 2015, but we found that there are regional differences. So, if you bought celery or kale or broccoli in Dallas, versus New York, L.A., Raleigh or Chicago, there's as much as a 100-fold difference in the amount of nitrate in that green vegetable.

Rip Esselstyn:

That's kind of frustrating.

Nathan Bryan, PhD:

It's farming practices. It's the amount of nitrogen in the soil. It's the time of harvest. There are many things. So, those are conventionally grown. And then if we also tested these against organically grown vegetables, which everybody thinks is good, they're good because they're free of pesticides, herbicides and all that, but the problem is we found that they have about 10 times less nitrate than conventionally grown.

Rip Esselstyn:

Why is that?

Nathan Bryan, PhD:

Well, because I think to get an organic label, there's restrictions on nitrogen-based fertilizers you put in the soil. So, you can add compost, you can add manure, all this, but there's no standardization of nitrogen in the soil. So, when soils become depleted in nitrogen, then there's less nitrogen for the plant to take up. There's less nitrate in the vegetable when you eat it. So, organic is good, that is eliminating some bad things, but organic is not so good in the fact that it's very difficult to eat enough organic vegetables to get sufficient nitrate to fuel this nitric oxide pathway. So, that's one, there's no standardization.

Nathan Bryan, PhD:

So, just because you're reading a lot of kale or broccoli or celery, it doesn't necessarily mean you're getting sufficient nitrate to produce the vascular effects of nitric oxide. So, that's one. That's a huge problem. There's a whole field of agronomy that has to do better on standardizing that process. And then number two-

Rip Esselstyn:

It would be nice to know, wouldn't it, if you know when I'm picking up my bunch of kale, right? If there was a sign that let me know roughly how much nitric oxide was in this?

Nathan Bryan, PhD:

That's right. Well, it's really nitrate, is the stable quantifier molecule.

Rip Esselstyn:

Okay. Sorry, sorry, yes, yes, yes, nitrate. Yeah.

Nathan Bryan, PhD:

There has to be some standardization of that, because the other important thing is that many other nutrients, micronutrients and vitamins that are assimilated into vegetables require nitrogen. So, if the soil is deficient in nitrate, that vegetables going to be deficient in nitrate, but it's also going to be deficient in things like chromium, manganese, magnesium, these trace minerals. So, that's a way that you could standardize, obviously, the nutrient density of a lot of these vegetables. So, that's number one. It's a high variability on the vegetables we eat. And then number two, nitrate is inert in humans. So, humans do not have the genetic or enzymatic capacity to metabolize nitrate into nitric oxide.

Nathan Bryan, PhD:

So, this is 100% dependent upon bacteria, primarily oral bacteria, and some gastrointestinal bacteria that we're finding as we go from the mouth all the way down to the anus. We can interrogate this system, but here's the problem. There's 200 million Americans that wake up every morning and use an antiseptic mouthwash. That is doing more harm than good. I think it's with good intent because people don't want to wake up with bad breath. We've published the facts that when you use a mouthwash, your blood pressure goes up. This is a fundamental problem in American society, because two out of three Americans have an elevation in blood pressure. That's the number one modifiable risk factor for heart disease.

Nathan Bryan, PhD:

So, the fact that you use mouthwash and your blood pressure goes up told us that there's an important connection between the oral microbiome and systemic blood flow and blood pressure regulation. And then the other thing is another 200 million Americans are on an antibiotic in any given time in the year. So, systemic antibiotics kill the good bacteria. So, this two electron reduction of nitrate to nitric oxide or nitrite that happens in the oral cavity is disrupted by antibiotics and mouthwash.

Rip Esselstyn:

Which more than 50% of Americans are on at any given time.

Nathan Bryan, PhD:

That's right. So, you can be doing all the things that you're supposed to do. In fact, I was on The Doctors show a couple of months ago, where we recognized that if you use mouthwash, you actually lose the vascular benefits of exercise. So, think about this, you could be doing everything that we've known has been healthy for hundreds of years, modern exercise and a plant-based diet. But if you're using mouthwash, you're not going to get any of the vascular benefits of either of those. So, that's a fundamental, I think, groundbreaking observation. I think it's the reason that some people respond to a plant-based diet and they can lower their blood pressure. Other people, you don't see any change in blood pressure.

Rip Esselstyn:

Right, that's fascinating. So, what is the solution there then when it comes to the mouthwash, just brush your teeth? Can you brush your teeth? Is there anything with fluoride?

Nathan Bryan, PhD:

No, I'm a big proponent of brushing your teeth. Brushing your teeth, but you have to use a fluoride-free toothpaste, because-

Rip Esselstyn:

Fluoride-free toothpaste.

Nathan Bryan, PhD:

Yeah, because fluoride is an antiseptic, antimicrobial. It's also a neurotoxin. So, yeah, I tell people brush your teeth, brush your tongue. The bugs that we're interested in that are responsive of this are on the dorsal part of the tongue.

Rip Esselstyn:

So, meaning what?

Nathan Bryan, PhD:

Meaning, the very back of the tongue.

Rip Esselstyn:

The back of the tongue.

Nathan Bryan, PhD:

Near the gag reflex. So, you can brush your tongue, but just don't gag yourself. Why are you doing that? So that's an important consideration. And then the other huge problem is... So, that gets us from nitrate to nitrite. To get us from nitride to nitric oxide require stomach acid. We've got over 200 million Americans that are using antacids. That's just prescription proton pump inhibitors. It's very difficult to quantify the amount of over-the-counter purchases for things like Prevacid, Prilosec, these antacids for people that have reflux disease.

Rip Esselstyn:

So, does that then wipe out the gastrointestinal...

Nathan Bryan, PhD:

You completely eliminate the blood pressure lowering effects of both nitrate and nitrite. These drugs also further inhibit the vascular production of NO. So, if you're on antacid, particularly a proton pump inhibitor, like omeprazole, first, they were prescription-only drugs. Now, you can buy them over-the-counter. But those basically shut down nitric oxide production from both pathways. Now, we've known for probably five or six years that people who have been on antacids for three to five years have about a 35% higher incidence of heart attack and stroke. No one made that connection because what the hell does stomach acid having to do with heart attack and stroke? Well, now we know it's a nitric oxide-related phenomenon.

Rip Esselstyn:

Wow.

Nathan Bryan, PhD:

So, 200 million people use antacids. Two hundred million people use proton pump or mouthwash, and other 200 million people are using antibiotics. That's more than the population of the US. Now, there's some overlap in those obviously, but what that tells us is that no wonder, it's not a surprise to me that cardiovascular disease remains the number one killer of men and women worldwide. It's not surprising to me that two out of three Americans have an elevation in blood pressure. Over 50% of the man over the age of 40 reports some degree of erectile dysfunction. It's a vascular problem. It's loss of nitric oxide. I think the numbers are probably close to 75 or 80%.

Rip Esselstyn:

That's over 40.

Nathan Bryan, PhD:

Over the age of 40.

Rip Esselstyn:

Over the age of 40. If I'm not mistaken, the one area of the male anatomy that has more endothelial cells per square inch than any other is the penis.

Nathan Bryan, PhD:

Yeah. So, to get an erection, that's basically an engorgement of blood flow. To get blood flow, you have to have a dilation of those blood vessels. To have a dilation of the blood vessels, you have to be able to make nitric oxide. You can't make nitric oxide, none of that happens. It's the same thing. It's not just men, it's the women and the clitoris. It's a highly vascularized organ. For women to have an orgasm, they've got to have an increase in pressure. That increase in pressure come from an increase in blood flow. That increase in blood flow comes from nitric oxide. You can't make nitric oxide, none of that happens.

Rip Esselstyn:

So, let me ask you, Doctor. So, let's say that I was a 48-year-old male coming to you with erectile dysfunction. I'm currently eating the standard American diet, using mouthwash. I'm on antacids, a little bit of antibiotics. What prescription would you give me to try and get back my virility?

Nathan Bryan, PhD:

Well, there's no prescription that can overcome physiology, right? Prescription drugs are typically inhibitors of certain biochemical reaction or stimulators of some enzyme that's probably not working. So, what we have to do and no matter what the clinical presentation is, my philosophy is the chronic disease is caused by two things and two things only. Number one, your body is missing something that it needs. Number two, your body is exposed to something that it doesn't need.

Nathan Bryan, PhD:

So, then we have to just go off the list. Okay, for taking mouthwash, you have to stop. If you're taking antacids, you have to stop. If you take any of these things that disrupt nitric oxide, if you're not getting up and moving and having physical exercise, then you have to get your body moving. So, that's kind of the process of eliminating the things that are disrupting nitric oxide production. Now that those kind of



unlock the brakes, what can we do to stimulate and digest NO production? So then, I would say you have to exercise.

Nathan Bryan, PhD:

I would recommend a plant-based diet that's enriched in inorganic nitrate or there's some technology on the market that's very effective supplementation that's been shown in peer reviewed, randomized placebo controlled clinical trials to restore nitric oxide production. So, that's kind of the path that I would take. Once you restore nitric oxide production, you gain the ability to regulate blood flow. Erections get better in both men and women. Blood pressure becomes more normalized. So, everything works better. If you can't get oxygen and nutrients to every cell in the body, that cell is going to become dysfunctional. When those cells become dysfunctional, the organ and the tissue fail, and that's the basis for disease.

Rip Esselstyn:

Let's back up just for a second. What in the world got you so passionate about nitric oxide that you made this your kind of, up to now, your life's work?

Nathan Bryan, PhD:

That's all I've done in my 20 years of academia. It happened when I was a student at LSU School of Medicine back, I guess in 2000. This was a couple years after the Nobel Prize was awarded. Louis Ignarro, one of the gentlemen who shared the Nobel Prize, came in, gave a lecture to the student body at LSU Medical School. Louis told us the story of his discovery of nitric oxide. And then I had a chance to have dinner with him that night and asked some fundamental questions about what is this nitric oxide molecule and why is it important. He told me that he was still quite surprised that a Nobel Prize had been awarded, number one. And then number two, that he actually shared the Nobel Prize. This was, I guess, right in 2000, 2001.

Nathan Bryan, PhD:

There were no technologies to detect or quantify nitric oxide in humans or even animals for that matter. And then number two, no one knew how to correct this insufficiency. So, he thought, there's kind of this great blue ocean out there of a lot of unknowns. For me, that was eye opening and important, because I recognize them that if we could figure out how the body makes nitric oxide, what goes wrong in people that can't make it, and then hopefully, have the technology to restore or repair these pathways in the human body. That if what he was telling me nitric oxide did and was, it would transform public health.

Rip Esselstyn:

So, you kind of took that as a challenge to go forth and find those answers.

Nathan Bryan, PhD:

Yeah, so basically all my PhD work was on analytical methods to detect and quantify nitric oxide in biological systems. Once we accomplish that, then we also had the tools to start to develop nitric oxide-based therapies. That led me to Boston University Medical Center as a Fellow, spent a couple of years there. And then I was recruited by Ferid Murad, one of the other gentlemen who shared the Nobel Prize to join faculty at U.T. Medical School in Houston. So, that was important, because Dr. Murad had a drug discovery program at U.T. This was about, I guess, eight years after he won the Nobel Prize. So, we were

tasked with trying to develop nitric oxide-based therapies. I found it fascinating because Dr. Murad had won the Nobel Prize for the discovery of nitric oxide, but yet he had no methods to detect nitric oxide.

Nathan Bryan, PhD:

So, when I joined faculty there, I had the only instrumentation that can detect and quantify nitric oxide. So, then we got busy and found out these compositions of matter that would generate nitric oxide. We knew how much nitric oxide a normal healthy human being made over 24 hours. So, we could dial in that level of nitric oxide. We refined this over period of 10 years or so and really get to a technology that does two things.

Nathan Bryan, PhD:

Number one, if your body can't make nitric oxide, we do it for you. And then number two, it really fixes the reason your body can't make nitric oxide, even in the face of antiseptics or antibiotics. So, it overcomes a lot of the deficiencies or a lot of the hurdles that we as ourselves put on ourselves because of the things we do. But I think still getting back to the physiology and biochemistry of nitric oxide. The best approach is to eliminate or remove the things in your life or body that are disrupting nitric oxide production. And then giving the body what it needs to make its own nitric oxide. That's the best approach. There's no better safety profile than that, and it works.

Rip Esselstyn:

So, I think you mentioned earlier on the endothelial cells. My father is a huge fan of the endothelial cells.

Nathan Bryan, PhD:

Yeah, very important.

Rip Esselstyn:

The endothelium, which as you, I mean, explain, I think is the innermost lining of all of our blood vessels, right? Is this where a lot of nitric oxide is produced from the endothelial cells?

Nathan Bryan, PhD:

It is. So, we've quantified this, about 50% of our nitric oxide comes from the endothelial cells. As I mentioned, 50% of that goes away with time. So, that's the reason for age-related cardiovascular disease.

Rip Esselstyn:

Can I just stop you?

Nathan Bryan, PhD:

Sure.

Rip Esselstyn:

So, I'm a five-year-old, right? Just by being a human being and having endothelial cells coursing throughout my body, are they just naturally producing nitric oxide just all day long?

Nathan Bryan, PhD:

As long as that five-year-old is eating a decent diet, is active. But if you've got an obese five-year-old that's sedentary, that's eating chips and cookies and sodas all day, he has probably the endothelial health of a 50 or 60-year-old. So, that tells us really the damning effects of lifestyle on endothelial health biology.

Rip Esselstyn:

Okay. So, let's say I'm that five year old that is eating really an atrocious standard American diet, how quickly can I turn it around by not disrupting the pathways and eating the right things and all that, kind of turn it around super quick?

Nathan Bryan, PhD:

Yeah, usually, it happens in a matter of days. I mean, our body's very resilient in the fact that it wants to do its job. The cells want to do their job. You have to give them what they need to do their job and get the stuff out of the way that's inhibiting them to their job. So, when you change your diet... I mean, it's similar to smoking. You can stop smoking and see the benefits within 24, 48 hours later in terms of how you feel, how you're breathing. A lot of that are basket of related effects. So, same thing with diet, if you eliminate all the postprandial inflammation that occurs from eating a lot of processed, nasty foods that causes endothelial dysfunction, then you don't get that inflammatory response. Inflammation is the key driver of disease.

Rip Esselstyn:

As I'm sure you may or may not know, we are not fans of meat, right? Animal byproducts, we feel like they're inflammatory. They injure our bodies at a multitude of levels. Are you a fan of animal products? I mean, if I came into you and I had low nitric oxide, would you say, "You know what? Go easy on the meat and really bump up the fruits, vegetables, green leafies"?

Nathan Bryan, PhD:

Well, for me, it's a balance. I mean, personally, I'm a meat eater, but before I eat meat, I always eat a salad. I think these social norms are really preparing the body for this postprandial oxidative stress that occurs from processing animal proteins. I mean there's some postprandial inflammation and oxidative stress from digesting any protein whether it's plant-based or animal based. The problem with most Americans isn't that they're overeating meat. It's they're undereating vegetables.

Nathan Bryan, PhD:

So, for me, you get a good mix of micronutrients and vitamins from a balanced diet. There are certain things that are in animal products that aren't in plant-based diets. So, you get a couple of options. You can supplement what's missing, which I think is very important, or eat a balanced diet. But I think there is no substitute for a balanced diet and moderate physical exercise. People are looking for a pill they can take to overcome that, and it doesn't exist. It won't exist.

Rip Esselstyn:

So, I'd love in this book, Nitric Oxide Solution, right? The NO Solution, you talked about some really smart methods to increase your nitric oxide production. I'd love to throw out a couple that you write about, and then if you could just expand on that.

Nathan Bryan, PhD:

Sure.

Rip Esselstyn:

So, the first one you talked about is breathe deeply, sounds pretty simple.

Nathan Bryan, PhD:

It seems like a simple exercise, right?

Rip Esselstyn:

But I don't think enough people are doing it.

Nathan Bryan, PhD:

Well again, that's very important. But the sinus epithelial cells contain this enzyme, nitric oxide synthase, just as the endothelial cells in the lining of the blood vessels. So, if that enzyme is dysfunctional in the endothelial cells, the same conditions exist that's going to make it dysfunctional in the epithelial cells. So, deep breathing is really not going to give you the optimal nitric oxide effect until you recouple that enzyme and make it functional. So, that's number one. Same thing, if you eat a plant-based diet, but you're using mouthwash, antibiotics, you're not going to get the benefit of it. So, very similar analogy.

Nathan Bryan, PhD:

But here's the deal if you know that enzyme is working or you employ the strategies that restore endothelial function, then simply deep breathing through your nose activates the mechanoreceptors on these epithelial cells and generates nitric oxide. That's why in those patients, simply deep breathing can lower your blood pressure.

Rip Esselstyn:

Can you give me an example, like how often, I'm breathing in through my nose, out through my mouth?

Nathan Bryan, PhD:

Yeah, if you do that, like 10 times in a 5-second interval, like breathe in for 5 seconds, hold it for a second, and then exhale for like 5 to 6 seconds. You can do that 10 times. That's been shown to be very effective at lowering blood pressure, provided that enzyme is functional that makes nitric oxide.

Rip Esselstyn:

Okay. All right, hydration.

Nathan Bryan, PhD:

Again, there's no substitute. I mean, if your volume depleted and your sales are concentrated, not just in toxic byproducts, it causes cells to be dysfunctional. So, you have to hydrate but you have to drink good water. Most water is toxic. I don't recommend anybody drinking municipal water. It's got fluoride in it, it's got chlorine in it, it's got drug metabolites in it. So, you're getting a lot of estrogens in the water. So, public water is made basically for safety and antimicrobial. They don't test for a lot of these drug metabolites that we urinate or defecate out that people are taking.

Rip Esselstyn:

What do you recommend?

Nathan Bryan, PhD:

I highly recommend a home water purification system that takes out the bad stuff, the chloride, fluorine, drug metabolites, and basically, puts back the trace minerals, this natural film in water.

Rip Esselstyn:

All right, and then do you recommend a certain quantity of water, or is it just depend upon how active you are?

Nathan Bryan, PhD:

Everybody's different. It's hard to make a one-size-fits-all for anything. I drink probably a gallon a half, two gallons of water a day, but I'm active. I work out. I sit in a sauna, so I sweat. So, I have to rehydrate.

Rip Esselstyn:

I'm going to be getting to that. Again, these all sound like pretty simple solutions here, but so we started with breathe deeply. Then we had hydration, good sleep.

Nathan Bryan, PhD:

Good sleep is important. Sleep is when our body heals. So, if we don't get good sleep, our body doesn't have the chance to heal. It doesn't perform as optimally as it should. And then the other important component of sleep is people with obstructive sleep apnea, hugely increases your risk of heart attack and stroke. So, that pathway that makes nitric oxide in the lining of the blood vessels requires oxygen. If you're hypoxic during your sleep because you're not breathing, then your body can't make nitric oxide. It puts you at risk for cardiovascular disease. So, again, there is a bonafide mechanism of action of why using proton pump inhibitors leads to a heart attack and stroke. There's a bonafide mechanism of why having sleep apnea leads to heart attack and stroke. It's all around nitric oxide.

Rip Esselstyn:

Do you have any recommendations for people to get a really good night sleep?

Nathan Bryan, PhD:

85% of Americans are deficient in magnesium. Magnesium involved, I think 187 biochemical reactions. Magnesium is calming. That's why people take 500 milligrams of magnesium every night before you go to bed. If you're like most Americans, you're deficient. So, it's going to provide you a missing nutrient. Two, it's calming, so it'll help you sleep better. And then you have to turn off your phones, turn off exposure delights, artificial lights. That's not how our bodies evolved to sleep. We have to have a down period to prepare a body for sleep.

Rip Esselstyn:

I love a cool environment. I also [crosstalk 00:36:24].

Nathan Bryan, PhD:

I sleep at 65, 66 degrees at night.

Rip Esselstyn:

Yeah, yeah. You talked about this earlier a little bit, but good bacteria. I think that maybe around that would be everything that people were doing inadvertently with the mouthwash or the fluoride toothpaste, with the antacids that are basically wiping out the good bacteria and preventing that... What would you call it, that reaction to occur?

Nathan Bryan, PhD:

It's dysbiosis. We've become a germaphobic society, especially now in this age of Coronavirus and all these rapid epidemics of infectious bacteria or viruses. So, everybody's using mouthwash, everybody's using antibacterial. So, people bathe two to three times a day, no one sweats, no one gets dirty. There's consequences to that, because the bacteria that live in and on our body outnumber our own human cells, 10 to 1. Most of these bacteria are in and on our body to do things that we as humans can't do or haven't yet evolved to do. So, there's always collateral damage of this.

Nathan Bryan, PhD:

So, yeah, you want to be free from infectious and pathogenic bacteria, but the collateral damage of that is you're killing the good guys. The good guys are providing your body with something that it needs, right? So, you can't do this. I mean, if I get septic, I want an antibiotic. I think it's a lifesaving procedure and very important discovery. But overusing antibiotics, using mouthwash, using antibacterial soap, lotions, bathing two to three times a day, there are consequences to them. It's known that people who grow up in a rural environment have less allergies. They're typically more healthy than people who live in an urban environment.

Nathan Bryan, PhD:

I live out on 15 minutes way out in the woods on hundreds of acres, and I'm quite observative. So, I've noticed growing up around horses and cows and dogs that if you bathe your dog or your horse, what's the first thing they do?

Rip Esselstyn:

Roll in the dirt.

Nathan Bryan, PhD:

They go roll in the dirt, right? Because they recognize innately that you've just removed a lot of the good bacteria from their body to the soaps and shampoos. So, what they do, they go out and reinoculate themselves in the dirt. So, that's a very important observation. Sweating, I think, is an overlooked thing. No one sweats anymore. We get in our airconditioned house, and travel in airconditioned car or airconditioned office, and come home. One of the main routes of exposure of toxins is through sweating.

Rip Esselstyn:

Yeah. We had a woman on the first season of Plant-Strong, Dr. Robynne Chutkan who is a gastroenterologist. Her motto is to eat clean, live dirty.

Nathan Bryan, PhD:

Yeah, I like it.

Rip Esselstyn:

Kind of a little bit like what you were just saying there.

Rip Esselstyn:

As Dr. Bryan says, dogs and other animals innately know how to give their bodies what they need by rolling around in the dirt. The same goes for their food, which is why we're proud to partner this season with Wild Earth. Animals know better and they deserve better, which is why Wild Earth dog food is packed with only clean protein sources and easily digestible ingredients for superior gut health, no junky meat products here. Scroll down to view the show notes or visit [plantstrongpodcast.com](http://plantstrongpodcast.com) and click on the Wild Earth banner to claim your exclusive offer for up to 50% off your dog food purchase.

Rip Esselstyn:

If I'm aging, let's say I'm in my 60s, 70s, but I'm also eating this way and eating let's say... My dad's protocol for his patients is six to seven basically fist-sized handfuls of some sort of dark green leafies every single day. Now, I don't believe ever, he had the knowledge about organic versus conventional and the difference there, but let's say you were doing the conventional, you're doing everything correct. If I'm 60, 70, is there a potential that I could have the nitric oxide production of a healthy 20, 30-year-old?

Nathan Bryan, PhD:

That is very possible provided you're not doing the things that disrupt that metabolism into nitric oxide. I think that's the reason that you see such a disparity in 70 to 80-year-old people. You get some 70, 80-year old's who are rolling in a wheelchair on oxygen, completely horrible quality of life. To the country, you get 60, 70-year-old guys who are playing golf every day. In fact, I just played golf with an 85-year-old in West Palm Beach, and he still drives about 340 yards.

Rip Esselstyn:

Wow.

Nathan Bryan, PhD:

It's remarkable. But he's active. He eats a good diet. He does a good clean life. That's the difference. So, for me, it's not about the quantity of life. It's the quality of life. I think if you do the right things, you can have both.

Rip Esselstyn:

Right. So, you mentioned this 84-year-old driving the golf ball 340 yards. So, as an athlete, right, I've been an athlete my whole life, do you feel like... I guess it's nitrates and nitrites that can produce nitric oxide in me would be considered a performance enhancer?

Nathan Bryan, PhD:

No doubt about it. I mean, the clinical published, randomized controlled trials tell us that. In fact, your ability to generate nitric oxide, which is measured by plasma levels of nitrite, actually predicts how well you can perform. So, if you supplement this or titrate your blood levels up of this, it's been shown to enhance performance. So, there's a couple of ways to do this. Young, healthy people or well-trained

athletes, when you begin to exercise, that stimulates nitric oxide production. That's why exercise is medicine.

Rip Esselstyn:

So, it's bidirectional.

Nathan Bryan, PhD:

It's bidirectional. There's a critical cross point here. That when you reach your anaerobic threshold for the cells in the blood vessels to make nitric oxide, you need oxygen. So, when you run out of oxygen when you're exercising, which is the anaerobic threshold, then nitric oxide production in the lining of the blood vessel shuts down. So, then that's when you run out of fuel typically. You switch to this anaerobic metabolism, lactic acid builds up. That's the whole cycle of performance.

Nathan Bryan, PhD:

But what we've recognized that if you can titrate your levels up prior, that when that pathway of nitric oxide stops working, then this reservoir of nitrate and nitrite can be reduced to nitrites, specifically under low oxygen. So, you've got a buffer system, and that's the buffer system that's really the difference between winning and losing, especially in the Olympics.

Rip Esselstyn:

So, have you quantified this as far as let's say I've got a big workout tomorrow that I want to get ready for, how many milligrams I want to do? How many hours before and how many days before do I want to be ramping it up?

Nathan Bryan, PhD:

So, we have a technology that actually generates nitric oxide gas. We published this in a peer reviewed journal that three minutes before a time trial on a bicycle, that if you take that 20 minutes before your exercise, you can increase your time by 3%.

Rip Esselstyn:

That's phenomenal.

Nathan Bryan, PhD:

I mean, it's truly the difference between first and last. But again, it depends on the type of activity you're going to do. So, the metabolic requirements of a time trial are much different than say resistance training or high intensity interval training. So, there's protocols being developed now. So, if you want to utilize nitrate as a substrate, that takes 90 to 120 minutes to go through this interior salivary circuit to be activated by the bacteria, to swallow it, generate nitric oxide in the fluid of the stomach. So, for that protocol, if it's just nitrate and you have to take this about an hour and a half to two hours prior.

Nathan Bryan, PhD:

But if you're using mouthwash, you're using antibiotics, you can't make stomach acid. Then you're not going to the performance enhancing benefits of that. But nitric oxide or nitride per se, you can take 5 to 10 minutes before and that provides that buffer or reservoir that will allow you to extend that anaerobic threshold and perform better than your competitors.



Rip Esselstyn:

So, to the best of your knowledge, do you know many sports teams or athletes that are supplementing with some sort of beet powder or beet juices and stuff like that?

Nathan Bryan, PhD:

I developed a commercial beet product and a technology. We have close to 200 sports teams that use it both professional in NCAA, from NFL, all NCAA programs including University of Texas here, MLB teams, NBA teams, hockey teams.

Rip Esselstyn:

Wow.

Nathan Bryan, PhD:

In fact, the entire US Olympic team in 2016 were using our technology.

Rip Esselstyn:

So, the cats out of the bag.

Nathan Bryan, PhD:

Cats out of the bag. At first, it was as anybody competitive, people that were using our products didn't want their competitors to know. But then it became aware because these sports dieticians, speak, go to these conferences, and then they let the cat out of the bag. And then we've got these other sports dieticians who go, "Hey, we heard so and so was using this, we need this. We hear that it's a game changer."

Rip Esselstyn:

How important do you think it is that people, let's say... I'll refer to my father and his protocol where he likes his patients to do six servings of green leafies a day. He likes them to chew them to masticate them, not to throw them in a blender and drink them as a smoothie. Do you think there's benefit to chewing as opposed to drinking?

Nathan Bryan, PhD:

No doubt, no doubt. So, there's several benefits. Number one, you just increase the surface area of the food particles you're digesting. So, you get better breakdown in the stomach and in the gastrointestinal tract.

Rip Esselstyn:

When you're chewing?

Nathan Bryan, PhD:

When you're chewing. Yeah, so you break them down into smaller particles. But then number two is you're increasing the resident time and the activation time for these bacteria to utilize the nitrate. In that particular protocol, you wouldn't necessarily have to wait 90 minutes until the entire salivary circuit puts it back in your salivary glands. There's enough resident time in there. So, if you tune in for say 60 or

90 seconds, those bacteria have that substrate available right then and there to start responding on it. So, it almost primes the pump if you will.

Rip Esselstyn:

Right, right. So, I think that I read that you are such a fan of NO, nitric oxide, that in your estimation, it should be considered a vitamin, right?

Nathan Bryan, PhD:

Yeah, so there's ways-

Rip Esselstyn:

or put on par with vitamin, right? Because if you're not getting enough, it causes diseases.

Nathan Bryan, PhD:

If you look at the definition of a vitamin that was defined, I think by Casimir Funk back in many hundreds of years ago, that it's produced naturally in the body, are found naturally in certain foods, and deficiencies cause specific disease. If you've replete it, the disease goes away. So, the best example is vitamin C. If you don't get enough vitamin C, you get scurvy. You can completely overcome scurvy by giving it back. That's the best definition of vitamin.

Nathan Bryan, PhD:

We think and there's evidence to support that if your body can't make nitric oxide, so number one, it's naturally produced. Number two, you can get it from your diet. But if your body's deficient in nitric oxide, you're subject to a host of chronic disease, including heart disease and stroke, number one killer of men and women worldwide. It's been shown that if you can replete and recapitulate nitric oxide base signaling, you don't get cardiovascular disease and many age-related diseases. I don't want to trivialize scurvy or beriberi or things like that, but deficiency of nitric oxide causes the burden of diseases that face Americans and people worldwide today. But I think it's not nitric oxide, the end goal is to get to nitric oxide.

Nathan Bryan, PhD:

So, vitamins are typically stable, right? So, I think we've always looked at nitrate is kind of what we call a pre prodrug or pre provitamin. Nitrite would be kind of the provitamin, and then nitric oxide is the active agent. There's evidence for that in physiology. We need vitamin D, but vitamin D is the metabolized by the bacteria in the gut to perform the active form or activated by ultraviolet light. Same thing with thyroid hormone, I mean our body produces T4 or we're given T4, allow the body to convert it, but it's an inactive hormone. So, nitrate would be like T4, nitride would be like T3 active hormone, nitric oxide is BT2. So, that's how the body works.

Nathan Bryan, PhD:

So, this isn't foreign to physiology. But I think what we have to do is really understand how can we replete this activity through the diet, optimize our own systems to utilize that to generate nitric oxide. That includes eating a good diet but eliminating the bad stuff that's in our body that's inhibiting this metabolism.

Rip Esselstyn:

Yeah, yeah. I want to show you this photo. I don't know if you've seen this or not, this is from my father's book.

Nathan Bryan, PhD:

Yes, I've read that book.

Rip Esselstyn:

Okay. This is one of his patients, you can see this is the left anterior descending artery. I'll put this in the show notes on the podcast for people that are listening so you can see it. But this is two and a half years later. This is before my father kind of knew about nitric oxide, because as you can see here, this is in 1996 to 1999. My question to you is do you think that this reversal was able to happen just because he was eliminating kind of all, at the time, the foods that he believed were injuring the endothelial cells? And then just because this is such a heavy fruit and vegetable-based diet and obviously green leafies, he was able to basically, metabolize away the plaque formations and then restore the body's ability to produce nitric oxide.

Nathan Bryan, PhD:

I don't argue with data. Obviously, data are open to different interpretations, but the data and the fact that you can reverse heart disease with this is very profound. So, what I like to do is I like to start with things that work, and then work backwards, and figure out the mechanism to where you can make it actually better. I think that's why basic science today in today's culture and academia doesn't work, because people try to find their favorite protein or favorite molecule or favorite enzyme and make it fit into a biological physiological system. It's like putting a square peg in a round hole, but I think if you start with what works and work backwards, I think to answer your question, there are a number of things that are happening there.

Nathan Bryan, PhD:

Number one, when you eat a plant-based diet, nitric oxide is a very important component to that. But there's also other micronutrients that were probably missing in their previous diet that they're now getting. But to me, it goes back to the basis of everything that I consider. It's your body heals when it's given what's missing and you eliminate what's inhibiting the process.

Nathan Bryan, PhD:

So, I think a plant-based diet probably provides a lot of that benefit, not only are you getting a lot of fiber and other micronutrients in there; but provided your body has the systems intact, it's going to utilize the nitrate from that plant-based diet to generate nitric oxide. We know nitric oxide can reverse plaque deposition, lead to reverse lipid transport, clean up blood vessels, make them pliable, functional. It would explain that data 100%.

Rip Esselstyn:

Yeah. Well, I mean, I think that they should rename nitric oxide to Nirvano. Instead of Nirvana, Nirvano.

Nathan Bryan, PhD:

That's true.

Rip Esselstyn:

I mean, it sounds like, it is, it is miraculous. I think more people need this information, know what they can do to make sure they're not disrupting the NO pathways, and doing everything they can to bump up their production of it. I think it's really phenomenal that you have devoted your life's work to NO. I think what we want to do is we want to say yes, to NO, right? Yes to NO.

Nathan Bryan, PhD:

Yeah. I think all of us look for a profession that we can change people's lives. I mean, I think a lot of people are motivated by that. I think very few people actually have the opportunity to do that in a real sense world. We can fake ourselves into saying that. So, I feel very fortunate and blessed to be in this field for 20 years and to contribute to the knowledge base of this. But I think this is certainly one of those scenarios where what you don't know can kill you, and it really doesn't have to be that way. This is very simple, common sense stuff. But I think it's education, lack of education, lack of awareness, that everybody has a good intent for the most part in doing the things that they do, but we have to recognize the consequences.

Nathan Bryan, PhD:

So, I think, again, if we begin to understand and appreciate how the body makes nitric oxide, what are you doing in your daily life that's disrupting this natural production of this molecule? Eliminate that, eat a good diet, get some exercise, and sweat. Yeah, it's pretty simple.

Rip Esselstyn:

We're now four months into this pandemic I caught up for a few minutes with Dr. Bryan just last week over Zoom about what he's doing as we speak using nitric oxide to treat symptoms of COVID-19, especially in our most vulnerable populations. No doubt, you're going to be hearing more about this subject in the very near future.

Rip Esselstyn:

Nathan, it's good to see you again. I think the last time that that we spoke, it was in person in Austin, and it was pre COVID-19. Actually, it was the very beginning of February before this was even really being talked about. A lot has happened since then, what's going on in your world?

Nathan Bryan, PhD:

Well, thanks, Rip. So, good to see you even though it's virtual. But yeah, we're living in a certainly different time than it was when we met face to face for the podcast. Before we know, four months into this COVID pandemic is that it is a serious virus. What we're recognizing is that there's certain populations that are more vulnerable to infection and then it happens to be the African American community. The data to me are really clear, because there's been known health disparities in the African American, even Hispanic population now for probably 50, 60 years. No one's addressed it.

Nathan Bryan, PhD:

Now, it's becoming very apparent with the COVID pandemic, because African Americans seem to be more susceptible to infection. Their rate of hospitalization is five to six times higher than any other racial or ethnic group. The severity of disease seems to progress much, much more rapidly. And then the risk

of death is anywhere from, some reports, it's four to six times higher risk of death. Some reports are showing 10 times higher risk of death for African Americans.

Nathan Bryan, PhD:

So, here's what's relevant for what we talked about months ago to now is that the health disparities of African Americans are due to lack of production of nitric oxide. We know now know that people that have comorbidities are really symptoms of insufficient nitric oxide production are the ones that suffer the worst severity of the disease, hospitalization, and death.

Nathan Bryan, PhD:

So, now we have a clear mechanism with of why African Americans are suffering from this as well as Hispanics, but we're really focused on the African American population. Now, we have ways and we're actually investigating this. So, we'll keep in touch and keep you tuned to this. But to me, this is very important because no one's addressed the health disparities of African Americans despite the fact that we now know a mechanism of action and it's the loss of nitric oxide production. Now, we have a chance to intervene and address this very vulnerable population at a very important time in our lifetime.

Rip Esselstyn:

Yeah, no, that's very exciting and very timely. Do you have any thoughts on what it is that that makes the African American demographic so vulnerable?

Nathan Bryan, PhD:

Yeah, it's genetic and lifestyle. So, there's a known G6PD deficiency in African Americans. About 10 to 12% penetrance, where in other populations that maybe is less than five. They're salt sensitive hypertension that seems to be more prevalent in the African American community. A lot of it's lifestyle, it's diet. So, all of those both from genetic, epigenetic, all the way down to physiological response to these environmental and genetic factors really makes them more susceptible to infection. The severity of disease progresses really, really rapidly. But most importantly, it gives us a chance to intervene and understand this from a mechanistic standpoint and really help this population of people.

Rip Esselstyn:

Fantastic. So, how have you been doing over the last three, four months with COVID-19? How are you and your family doing?

Nathan Bryan, PhD:

We're doing great. Yeah, it's been kind of a great reset button for me, because prior to this, I was traveling about 140,000 and 150,000 air miles in a year, gone every week, traveling, lecturing somewhere. So, I've gotten a lot of work done around the ranch. We're as secluded as you come. We're 800 acres out in the middle of nowhere in Texas and so we're secluded, we're isolated. We've had fun. We got a lot of work done and it gives me time to spend time with the wife and kids.

Rip Esselstyn:

Nice. Nice. Well, I really appreciate the quick update. We're going to obviously add this into the live episode that we have when we were together. But let me just sign out with a new sign off which is peace, Engine 2, nitric oxide.

Nathan Bryan, PhD:

All right. Thanks Rip.

Rip Esselstyn:

I want to thank Dr. Bryan for his groundbreaking and dedicated research for the last 25 years. When cells can't get oxygen, organs and tissues fail. That's the basis for most disease. But by following some of the advice in this episode, especially around chewing your greens on a daily basis, you can reverse this trend and turn your body into a nitric oxide machine.

Rip Esselstyn:

If you're one of the millions of Americans who rely on antacids, antibiotics, or fluoride on a daily basis, know that there is a better way. There's no prescription or medication that can overcome physiology. Once you restore nitric oxide production, everything works better. Make sure you visit the podcast page at [plantstrongpodcast.com](http://plantstrongpodcast.com) to learn more and download some of the key tips from today's jam-packed show.

Rip Esselstyn:

The Plant Strong Podcast team includes Laurie Kortowich, Ami Mackey, Patrick Gavin, Wade Clark, and Carrie Barrett. I want to thank my parents, Dr. Caldwell B. Esselstyn, Jr. and Ann Crile Esselstyn for creating a legacy that will be carried on for generations and being willing to go against the current and trudge upstream to the causation. We are all better for it.