DANNY LENNON: Now with that, let's get into today's topic of discussion. So without further ado, let me introduce Dr. Eric Trexler. Eric, thanks for joining me on the podcast.

ERIC TREXLER: Yeah, thank you for having me back. You had me on several years ago, I was wondering if I would ever get the return invitation but happy to get it?

DANNY LENNON: Yeah, I'm sure people have been eagerly waiting with holding their breath. So I am glad to bring that to them now. But yeah, you were one of the ones in the early stage, I think we were still in double digits in terms of episode numbers when you first came on. So we've of course, had the privilege of being able to meet in person since then, and actually talk as real humans, not just in podcast land. So that was nice. So hopefully this teases up well for a second episode.

ERIC TREXLER: Yeah.

DANNY LENNON: What I would like to start with is to maybe set the stage for some of the rest of this conversation. And it actually comes at a good time that recently on the podcast, we've talked about inflammation and tied into that topic often people hear about antioxidants or their importance or in some cases, maybe lack of, but oftentimes some of these terms need some clarification in in order for them to make sense, and I suppose antioxidants, even as a topic, or why they

might be important only makes sense in the context of first understanding oxidants, or at least other terms, people would have heard of free radicals, reactive oxygen species and so on. Can you maybe set the stage for us of what are some of those terms we need to be clear on?

ERIC TREXLER: Yeah. So just to give some background, a meta analysis recently came out that was looking at the effects of antioxidants on adaptations to training, both endurance training and resistance training. And when it came out, I said, I definitely want to dive into this literature and write an article about it for the Stronger By Science audience. And without question, this was the most frustrating and tedious article I've ever written academic or non academic. And the reason was, like you said, there are all these terms that get thrown around and rarely get really nailed down to a straightforward definition. And so if you're at the grocery store, you turn around some little juice drink, and it says packed with antioxidants. And you're going to see a bunch of buzzwords on there, and a bunch of specific names for antioxidants, but it really does before you get into that conversation, you have to take a step back and say, what is an oxidant? What is an antioxidant? And what where do these various components of food fit in with that antioxidant umbrella? And so oxidation that brings me all the way back to when I was 18 years old, in my first college chemistry class, right. So oxidation, chemical process characterized by the loss of an electron. So we start really simple, that's oxidation. And we have all different cells throughout the body that are susceptible to this oxidation and components of cells that are susceptible. And so what I do in the article is kind of walk through how all of these terms fit together; inflammation, oxidative, stress, antioxidants, all of them. But the general idea, just to give us like a starting frame of reference here is that we create these things that I collectively refer to as reactive species. But that includes free radicals, reactive oxygen species, reactive nitrogen species. We're going to just collectively call those reactive species. And it's normal that we create these. It's not just normal, I mean, it's necessary these are natural byproducts of metabolic processes in the body. And then of course, there are other ways that we can see

these increases in reactive species. So things like radiation exposure, cigarette smoking, air pollution, exposure to certain industrial chemicals. So there are some very necessary exposures to reactive species and then some that are unnecessary and would be ideally be avoided for a variety of reasons. But in any case, we have these reactive species and these are highly unstable molecules, and they wish to become stable. And so what they will do is interact with cells throughout the body if they're left unchecked, and they will induce these oxidative reactions, these transfers of electrons. And the reason we care about that is these oxidation promoting reactive species, they have the capacity to damage important components of cells. So they can induce protein damage, lipid damage and DNA damage. And so, under normal circumstances, these reactive species aren't really that problematic because they're kept in check. We kind of have this balanced system where, of course, we naturally expect things to increase the production of reactive species, but we can counter that by using our endogenous antioxidant system but also using some help from the antioxidants that we consume in the diet. The problem is when this balance gets skewed, particularly with the one that we see naturally occurring where people have medical issues related to it or recovery issues, in some cases, is when we see that oxidative these pro-oxidant reactive species are accumulating at a rate that our antioxidant systems cannot defend, cannot keep up with to kind of neutralize it. And so that's where we enter a state of what we would call oxidative stress. We've got this excessive accumulation and contribution from these reactive species that promote oxidation and we simply simply overwhelmed our capacity to actually deal with it effectively. Okay. So that's where we get into oxidative stress and like I said, antioxidants in the diet, of course, our endogenous antioxidant system is important but that's kind of an autonomous thing. We can do some things to influence it, but when people think of kind of managing oxidative stress, they initially think, okay, what can I do in terms of dietary antioxidants. That's kind of the most intuitive step. And that is another layer that causes a great deal of complication. And in my case, a little bit of frustration writing this article is you think dietary antioxidants.

So antioxidants is a huge group that you can split into natural and synthetic.

Now the natural antioxidants you can split those into enzymatic and non-enzymatic. Within the non-enzymatic natural antioxidants you have got some vitamins and minerals. You've got polyphenols, carotenoids, and some others. You can break down polyphenols and say okay, we got flavonoids, phenolic acids. We can break down flavonoids and say we've got anthocyanins. We've got isoflavones. So without getting too repetitive here I mean, I think there's been 4000, at minimum 4000 polyphenols identified, and that's just one sub-sub-subclass of antioxidants. So what's really frustrating for me as I go through and write this article is, I would like to say, here's what the antioxidant in the diet is and here's the appropriate dose. But to even embark on such a mission is it's a fool's errand. I mean the thousands of different compounds that fall under this umbrella necessarily require that you speak about the topic in somewhat general terms, which for someone like me is frustrating. And I think that feeds into why we see all these buzzwords. We see all this lack of clarity about the topic. But the general idea just to kind of wrap things up here we've got reactive species that are necessary. There are some important physiological processes that rely on some degree of reactive species being present and being produced. The issue comes when we have excessive reactive species that we can no longer manage with our natural antioxidant capacity. And when we see that imbalance develop we see excessive oxidative stress, which is associated with a bunch of bad things.

DANNY LENNON: Several points. I'm actually going to hopefully touch back on over the course of this conversation I want to get back to but just to lead off, you mentioned the detrimental impacts oxidative stress can have and again, just to kind of build on the fact that in our previous podcast episode, we were discussing inflammation. Can you maybe outline for people what that relationship between oxidative stress and inflammation looks like?

ERIC TREXLER: Yeah, so that's a good point. I did listen to your episode on inflammation. That was very good.

DANNY LENNON: Oh, thank you. Thank you. Appreciate.

ERIC TREXLER: I liked it a lot. So oxidative stress and inflammation. Sometimes you'll see them used almost interchangeably, which is not necessarily an appropriate way to view them. I think the most appropriate way to view them and contextualize them is that they are related in a bidirectional manner, but they are distinct concepts. So oxidative stress, certainly can induce inflammation. It can induce an inflammatory response. At the same time, in many cases, an inflammatory response to some type of insult or injury to the body in the process of that inflammatory response, we will see that part of that response is an acute localized increase in reactive species production. And so that's I think, where the confusion lies with getting those terms mixed up is that one can lead to the other and vice versa. So they are bidirectionally linked, but they are very much distinct concepts.

DANNY LENNON: The other thing that you would just mentioned in that initial answer was this idea that not only is it not problematic to have some degree of these reactive species around, in fact, it's necessary and can be productive. And so if we consider that they have some degree of physiological function, it seems to be that we're suggesting that having none at all is problematic. But having this overburden of them is also problematic. So maybe we think of that as a inverted U graph almost. Is that relationship than one of like a hormetic stressor that we're getting a benefit from having an acute increase in these around and then things come back down to baseline? Or is that an incorrect way to think of that?

ERIC TREXLER: I would say that's correct. Yeah. So a great example, I focus on exercise. That's what I do. So a great example is with exercise, right? So there are some remarkably invasive studies with like animal models and stuff where they will blunt the production of reactive species and and look at how that affects contractility of the muscle fiber. If we had absolutely no reactive species response to acute exercise, it would impair muscle contractility. We would not be able to optimally function in the context of exercise. At the

same time, if we look at experimental models where the the production of reactive species is excessive, and it's far too high, we also see that that has a detrimental effect on muscular performance, neuromuscular performance, and a more rapid onset of fatigue and disruption of contractility.

So it's exactly what you're describing there where we need some of this response, this reactive species response, but if we have an excessive response that is not kept within a working range, then we have negative effects on the other side of that inverted U shaped curve. So I think the way you put it is perfect and it's not just muscle contractility, I mean, reactive species have a number of different purposes in the body. They really relate to signaling responses, cellular signaling pathways, ion transport; a variety of really critical physiological functions that if we just said, hey, we've got this magic pill, and it makes sure you never create any reactive species, it would be obviously completely impossible to do such a thing. But even if you could, it'd be a terrible idea.

DANNY LENNON: So if we're going with the concept of there's a, for lack of a better term, a Goldilocks zone, that may not be accurate, but there's this range where having some degree of these free radicals or reactive species, probably more accurately present is required. When we know that hasn't been considered with the research on the impacts of antioxidant supplementation, what the current burden of those reactive species is at the time of supplementation, in terms of how that may impact the result we get.

ERIC TREXLER: I think if you look at the literature pertaining to training adaptations, I think you can get yourself to a spot where you say, yes, it does matter. And so the reason I say that, and we'll get into the details on this later, but you could make an argument that this antioxidant supplement strategies as they pertain to training adaptations look a little bit more favorable in older individuals and a little bit less favorable in younger individuals. And these are all in healthy populations. And I think you can intuitively kind of reason your way through it and say, well kind of a key characteristic of aging is that we do see greater baseline oxidative stress in most cases or kind of a, I'm going to make up a term here but like oxidative

tone, I guess. And so you could indicate that maybe because of that, we see that it is looks a little bit better in older individuals who are starting from a place where they do have a little bit, they have more reactive species to take care of in that scenario. Does that make sense?

DANNY LENNON: Yep. Yeah, totally makes sense. And I'm glad you were able to make sense of my very poorly constructed question but we got there. So, one thing before we dig into specific details, and I may actually be jumping the gun on this, because there may be a better more natural point later in the conversation. But it seems that exercise tends to have benefits for our health, surprisingly, and I think this is probably no different. So with regards to the benefit of exercise on our antioxidant system, what is that improvement that exercise can confer?

ERIC TREXLER: Speaking very generally, whether there are really good intervention studies looking at whether we're doing an aerobic exercise intervention or a resistance training intervention and oxidative stress can be measured in a number of different ways. But what we generally see from these two bodies of research collectively is when we initiate exercise, there is that reactive species response. We do see an acute instance of oxidative stress. Of course, it's manageable. We deal with it. But what we see is that over time, kind of a key adaptation to training again, whether it's aerobic or resistance training, is that we essentially bolster our endogenous antioxidant systems so that our antioxidant systems that are endogenous that are just kind of inherent to our bodies become more robust. They become more able to deal with these acute excursions in reactive species. And over time, we essentially increase the capacity of our endogenous antioxidant system. So I'm sure you could find a horrifically detailed paper to walk you through the biochemistry of how that occurs, but in terms of the take home point, that's pretty much where we get is we have an overall improvement in our natural kind of endogenous ability to handle oxidative stressors and what's important is that doesn't only confer protections to exercise induced oxidative stressors. That is something that we can keep with us and when we are exposed to some kind of excursion and reactive

species or some increase in oxidative stress, we are more able to deal with that generally speaking which is a very-very positive adaptation of exercise.

DANNY LENNON: So if we know there's going to be this acute spike in reactive species production at the time of exercise, but the fact of someone being trained or aerobically fit or just being generally healthier also probably is going to allow them to have this better antioxidant capacity to be able to bring that back down to baseline effectively rather than a chronically elevated reaction species burden. Are there any detrimental impacts that come from that increased production of those free radicals at that time or presumably, as long as it comes back down to baseline we're good.

ERIC TREXLER: Yeah, I mean, it'll come down eventually one way or another. But in terms of the acute impacts of that, we do see some what I would call kind of incorrect signs of what you're getting out of can that acute challenge of reactive species be potentially detrimental? I do think you could argue that there are some signs where you'd say, okay, well, that's probably generally related to this concept. So signs would be things like there have been some studies indicating that individuals after remarkably vigorous bouts of exercise are a little bit more susceptible to particular acute illnesses like respiratory infections, things like that. But something I very much hesitate to bring up, given the COVID situation I'm not talking about that at all. I'm talking about there's been some research indicating that for example, people who do a really intense marathon in the weeks following might get a little acute illness after just because their their immune defenses are dropped a little bit. We also see things that are very, very simple like that soreness that you feel after a workout that acute muscle damage, you could suggest that this reactive species increase could theoretically be linked to some of those factors like that that immune response to really intense exercise or the localized effects that we're seeing in muscle, because some of that oxidative stress can play into some of that muscle damage that we see after exercise. So there are instances where whether we want to fully place the blame on reactive species or not. There are certainly instances where that acute stressor induced by the exercise bout can lead to outcomes that you

could intuitively kind of link to this general biochemical chaos that occurs from unaccustomed exercise.

DANNY LENNON: That question was just a byproduct of thinking out loud more about for people who are training regularly healthy aerobically fit is the benefit they have, is that solely down to having this increased antioxidant capacity? Or is it theoretically also a case where even when they do have this very high burden of reactive species that their tissues are just more resilient to damage from that?

ERIC TREXLER: I would say that that is a multifactorial question that probably has a multifactorial answer. I think you could get down to the specific systems that adapt to exercise. I think there's several adaptations in place that do confer some of that resilience that you're referring to. I think the antioxidant capacity of the endogenous system is one of many adaptations that plays into what you're describing.

DANNY LENNON: Sure, and again, it was quite a mess of a question. So before derail this thing any further let me try and get things back on a more straight route. One thing you've already touched on, but I just want to make sure to revisit this because I think this is probably the crux of the issue why this gets brought up in relation to resistance training, at least is the line of thinking has previously been okay when we have these adaptations to training, we know there's this inflammatory response that's kind of part of driving the adaptation. And then there's been two sets of logic, right, there was this kind of logic? Well, we don't want this burden of reactive species. So we can maybe supplement at this time to try and reduce that. Then there's the counter argument that as well being well, we don't want to dampen that response because it's part of those training adaptations. So that idea that we should avoid acute, high antioxidant supplementation in that immediate recovery window after saying resistance training session. Is that an evidence based notion?

ERIC TREXLER: You know, it's really funny because the way you introduced the question was basically, there's these two ends of the spectrum, right? And we're talking

about fitness. So you can't be in the middle. It's gotta be either if we totally blunt reactive species production or effectively scavenge the hell out of it immediately. This is going to make us healthier, fitter, we're going to train harder, it's going to be great across the board. And then like you said, the other school of thought is, these reactive species have important cell signaling impacts and we need to make sure that we allow that response to happen so we can adequately challenge basically observe that challenge at a cellular level and then adapt to it. And I'm going to go ahead and just cut right to the chase. I have the least interesting opinion on this you could possibly have, which is right in the middle. I think some degree of an antioxidant response is important or I'm sorry, some degree of a reactive species response is important. I don't really think that this high dose antioxidant supplementation for training purposes. I don't think it's advisable but I also don't think it's quite as detrimental as people think. But anyway, to answer your question, is it evidence based? There is some grain of evidence that you could base it on, which is really, that tends to be the case with most pervasive myths about anything fitness related is not that it's totally out of left field, but there's something there, a theoretical kind of granule of truth that you can build a theory upon. And I would say this is one of those instances. So when you look at the literature, whether we're talking about aerobic or endurance type training or resistance training, there is evidence that high dose supplementation with things like vitamin C and E combined, it can interfere with some of the signaling events that we observe after exercise.

So in the case of endurance training, we'll see that some of the signaling pathways involved with mitochondrial biogenesis can be inhibited by this very high dose antioxidant supplementation. In the resistance training literature, they found a similar thing with some anabolic pathways. So some pathways associated with muscle hypertrophy. They are indeed blunted a little bit from this high dose antioxidant supplementation. And so I think if nothing else in intuitive extrapolation of that would be if I do this high dose supplementation, it's going to interfere with my endurance adaptations or interfere with my hypertrophy adaptations. But what's really

fascinating and like I said, there was a terrific meta analysis by Clifford and colleagues within the past year or so, that looked at this whole body of evidence of longitudinal training programs with high dose vitamin C and E supplementation. What's really fascinating is there appears to be a disconnect and what I mean is, we can see these acute effects on some of these signaling pathways. But the actual training adaptations themselves don't seem to be blunted to a very notable degree and they looked at things like VO2 max for endurance training interventions. For strength training interventions, they looked at strength and hypertrophy outcomes. And they did note in their findings, or I don't know if they noted this, but it's something you can see from their findings is that when it comes to my biases, I'm mostly interested in strength and hypertrophy. When it comes to the strength and hypertrophy literature, as I was alluding to earlier, for healthy people, you could maybe argue that there was a slight detriment in some of these studies, where hypertrophy was just maybe modestly blunted or attenuated in one of the measurements they took. So for example, if we looked at three different muscles, maybe one muscle, we did see that the results were significantly different in the antioxidant group versus the placebo group. But maybe the other two muscles were unaffected or were not significantly affected I should say. So in the younger folks who are healthy and fit and unlikely to have a high level of baseline oxidative stress, you could argue that maybe there was a very-very slight negative impact of this high dose supplementation. In the older samples that they looked at, you could argue that maybe there was a slight benefit, maybe. But again, I think the thing that really jumped out to me was that in my side of the evidence based fitness world I think it'd become very much accepted that high dose antioxidant supplementation will very severely blunt your gains to training, whether it's strength or hypertrophy, and I was very much surprised looking at the individual studies that it's not quite that straightforward. The result is not or the impact is not enormous and I guess I was more surprised by the fact that it is not consistent. There's, like I said, a study here or there showing something but nothing huge, or even within a study, we found that one measure was affected, but not the other two

or three. And so, just to kind of summarize where we're at with this literature, I think there are the people arguing you got to do everything you can. If you take these antioxidant supplements, it's going to take your training to the next level. You got to blunt all the reactive species you can and you are going to improve more throughout the course of a training program. The evidence doesn't seem to support that. However, there's also that school of people that school of thought where people are suggesting, if you do take these, you're going to bluntness reactive species response, that impact on cell signaling is going to totally ruin your strength and hypertrophy gains. The evidence doesn't seem to support that either. So my take on it, especially if you're relatively younger, healthier individual, body composition is in a range that you wouldn't expect a high level of kind of resting baseline oxidative stress, I view these high dose antioxidant interventions, particularly with vitamin C or E as there is some small risk of a modest impairment. I don't see it as something that is absolutely catastrophic. But more importantly, there's not a lot of evidence to support a notable benefit when we look at the actual training adaptations over the course of time. So if there's some slight risk for a modest impairment, and really, I just can't see any potential benefit from these high dose vitamin C and E interventions. My natural takeaway from that is probably that it's an inadvisable supplementation strategy but not as scary as I think a lot of people had in mind.

DANNY LENNON: Yeah, it's not that, it's having this big crazy blunting effect, but it's more if people are asking you the question, hey Eric, should I be worried about taking high dose vitamin C and vitamin E, the probably first response to say, well, why are you doing that? Like,

ERIC TREXLER: Exactly.

DANNY LENNON: Like, why would you do that after training. And I think one of the things about some of the reductionist thinking that can commonly occur with antioxidants but also other nutrients, and I definitely see it in relation to antioxidants when we discuss it in terms of health outcomes and chronic disease. One of the big areas where there's a disconnect is when we look at

these isolated supplements versus antioxidant rich foods and there's several reasons for this. This doesn't just play out with antioxidants. There's other nutrients with it, we see the same whether that's fish consumption versus Omega-3, so on, and I'm just wondering, given that you took your focus around the performance, exercise, hypertrophy, research, has there been much that's looked at impacts of using antioxidant rich diets as opposed to high dose supplementation? And if so, do we see differences there?

ERIC TREXLER: It's a really good point. I think probably in my opinion, one of the most unfortunate things about this idea becoming popularized that high dose antioxidants are going to kill your gains. One of the most unfortunate ramifications of that is I have seen some instances, I don't think it's super common, but I've seen some instances of people questioning if I want to be very proactive about my health and fitness, should I be limiting my fruit and vegetable intake near my workouts and my general idea when you're typing in a Word processor, and let's say you're using some some poor grammar, it won't auto correct for you, but it'll underline it and it also Like Danny, you should go back and check that sentence. I don't think those words go together the way you're trying to put them together. I think your brain should have a, an immediate underline function. Whenever you're saying, in the interest of my health and fitness, should I avoid vegetables, that should automatically be a huge red flag. So that that's my general take. But we do have studies that rather than looking at a super high dose of vitamin C in a pill, looking at juices and extracts from various fruits and vegetables. I'm sure there are studies out there looking at whole food interventions, but it's not an area that I've looked at a ton, but what I can say is looking at some of these kind of fruit or vegetable derived juices and extracts that are much more close to a physiologically possible intake of antioxidants, if that makes sense. So these kinds of juices basically make it such that we had a huge, but possible intake of fruits and vegetables for the day, not some insanely high mega dose powder of vitamin C. When we look at those studies, there's a couple important things that there aren't quite as many of them looking at hypertrophy outcomes. But

the ones that do exist we don't really see any notable blunting of hypertrophy. So that's a good thing or strength or hypertrophy, I should say. So that's a good thing. The other thing to keep in mind is, like I said, antioxidants, we're talking about thousands and thousands of different compounds and when we put them within a naturally occurring fruit or beverage matrix, like we would see in just a simple like tart cherry juice, for example. We're not just getting the one antioxidant that we think is important, right? We're not just getting the anthocyanin content or whatever the case may be. We are getting a very complex food or beverage matrix with countless potentially bioactive phytonutrients. And so to assume that we know all of the physiological implications of all of the naturally occurring molecules within that food or beverage matrix, that's a preposterous assumption. And so what we find is that when we do these supplementation interventions with these fruit or vegetable based extracts and juices, there are some fairly positive outcomes that have been observed. And I think some examples of these types of things with tart cherry juice, we've seen interventions with really solid enhancement of recovery from acute exercise stressors. With beetroot juice, we've seen pretty notable performance improvements, but again, it would be very reductionist to say that beetroot juice is an antioxidant supplement. There are antioxidants present specifically some polyphenols that come to mind. But we've also got nitrate. We've also got potentially some betaine or trimethylglycine. Beet juice, it has a lot of stuff going on in there. We've seen positive effects from things like pomegranate juice and pomegranate extract, watermelon juice. So there are studies looking at these, they're not necessarily whole foods, but they're a lot closer than a vitamin C pill at 1000 milligrams and we see positive effects on acute recovery outcomes, muscle soreness, blood flow during exercise. And like I said, we don't really have any evidence to suggest that they would impair training adaptations over time at this point. That could change. But for now, we don't have any evidence to suggest that would be problematic. And I think one thing to keep in mind is that some of these phytonutrients, antioxidants, these kind of naturally occurring antioxidant compounds that are present in these fruit and vegetable matrices. They appear to

potentially work via a mechanism that is distinct from a straight up vitamin C supplement and so that's something I touched on in my article. There was a really good narrative review paper within the past year by Ismael et al. It actually might have been a single author I forget, but the lead author's name is Ismael. And what they documented was the fact that these phytonutrients antioxidants probably work most directly by affecting the nerve two pathway NRF2 and so what happens is it they stimulate activity of that pathway, which stimulates activity of some of our endogenous antioxidant systems and our antioxidant enzymes that we have naturally present. Rather I guess the converse situation for vitamin C is that when we take this huge dose of vitamin C, we have a capacity to greatly increase plasma vitamin C levels. It can directly scavenge these reactive species immediately upon formation. And it's just not we don't really have that in check the same way that we have the capacity to manipulate our endogenous antioxidants systems via the nutritional supplementation with these different phytonutrients. So it's kind of a long winded answer. But the general idea is that you can make a mechanistic, very intuitive rationale for why some of these phytonutrients that are naturally occurring in the food matrices of different fruits and vegetables, you can make a mechanistic explanation for why they would be distinct from something like vitamin C. And then when you look at the actual interventions that use these different juices and extracts these phytonutrients have interventions that tend to have a lot of polyphenols, which is a kind of broad class, but they tend to have better acute effects and don't seem to have any potential, or we don't have evidence to suggest that they have a downside when it comes to training adaptations. So my general approach personally is I encourage people to eat a diet that is abundant in antioxidants, but no more abundant than they could actually achieve on planet Earth without some kind of mystery powder or potion. So I usually tell people, yeah, some kind of fruit extract, that's fine. But what I generally recommend doing is have a diet that's very rich in antioxidant heavy fruits and vegetables, ideally, a diverse intake so that you're getting a broad range of phytonutrients into the diet. And the first time I came on your show, we talked

about nitric oxide, right? I ended up doing a lot of my dissertation research on nitrate. And so people were saying, I've heard people say, well, should I supplement with potassium nitrate or sodium nitrate or this and that I said, eat some beets, eat some spinach, eat some celery. Best case scenario, you get a notable but fairly modest performance improvement. You might see your blood pressure drop a couple points things like that. Worst case scenario let's say I totally misled you and this nitrate did nothing for you. The only downside of that intervention is you just kind of accidentally stumbled upon a much healthier diet. Your diet is now rich in fiber, and fruits and vegetables, a variety of phytonutrients that for most of them we haven't even begun to understand exactly how beneficial they are in the body and exactly what they do. But it's really hard to go wrong with advising people to consume a diet that is very rich in a variety of fruits and vegetables. And I think that probably puts you in a place where you are likely to maximize the potential benefit some of these interventions, and I just can't, I can't fathom a downside to that type of intervention.

DANNY LENNON: And that's it. The more reductionist you go in that line of thinking, the more layers of complexity you introduce, and even if you're looking at a specific phytonutrient It's not like they have one biological role. So it may be different from what's been even examined in a certain context. But before we start wrapping up here, Eric, is there anything particularly important in this topic that I haven't got around to asking you or that you think you'd like to highlight to people?

ERIC TREXLER: Danny, you've said several things about your question for me throughout this interview. But here's a true story. I was on someone's podcast the other day and off the air, I told them, you are the second best interviewer I've ever spoken with. And that's a huge compliment, because you're only behind Danny Lennon. And I really mean that. I think you have done a terrific job. I don't think we've left out anything important, but I would like to maybe add one additional, two additional things. So one is about nitric oxide. So don't let me forget that Danny. The other is just a more general statement. I have learned

recently that I am very much an introvert. And I've been reading about what that means. And one of the notable things that I saw on a complete non-evidence based article about introverts is that they're better at writing out ideas than speaking them. So if you heard me say anything in this podcast and you thought, I think Eric Trexler is kind of full of it, check out the article. I think I lay out the ideas a little bit more concisely and coherently in the article. It's StrongerByScience.com/antioxidants. The other thing I wanted to add, like I said, my dissertation was on nitric oxide. I looked at citrulline malate. I looked at beetroot juice. That's naturally my bias is I think, nitric oxides is very cool. But I talked about some of those polyphenol interventions, or those more phytonutrient focused interventions. I think one of the things to keep in mind is, theoretically, you could suggest if you happen to use a nitric oxide supplement for performance purposes, so if you take citrulline malate, if you take some form of nitrate it's very possible that these antioxidant interventions, aside from their own independent effects, they probably work pretty synergistically with those types of interventions. So there have been some studies where they pair L-citrulline with reduced glutathione purely for its antioxidant effects because what we see is that antioxidants when consumed with some kind of nitric oxide booster antioxidants naturally reduced the conversion of nitric oxide to peroxy nitrite. And an extension of that is that they enhanced the bioactivity of nitric oxide. So if you're someone who is taking some kind of, doing some kind of intervention to increase your nitrate intake or citrulline intake or something like that, you might consider pairing it with some kind of source of antioxidants; specifically I think polyphenols are a great option and they tend to be naturally occurring well, which is fantastic. And I think a great example of that idea in practice is there is a I think there's one or maybe even two studies comparing a high nitrate just a normal beetroot juice supplement with a sodium nitrate dose, and they had the same amount of nitrate and they wanted to see is it really just the nitrate that's working here with beetroot juice. And what they found was the effects with the beetroot juice itself were slightly better than the sodium nitrate alone. I think a huge portion of that is due to the synergistic effect between nitric

oxide and antioxidants. So if you're listening along and thinking, I guess this means there's nothing interesting that can be done with antioxidant supplementation. I don't think that's the right takeaway, or just antioxidant interventions in general because like I said, it doesn't have to be a supplement. But if you're someone who's really intrigued with this idea of nitric oxide supplementation or I should say boosters of nitric oxide, you should take a close look at your antioxidant and taking your diet and whether you're achieving from food or supplement, it could be a very interesting opportunity to really maximize the potential benefit of any type of nitric oxide intervention.

DANNY LENNON: Yeah. And I think that's actually really important that you outline that we shouldn't throw the baby out with the bathwater. The takeaway is certainly not I can forget about this thing. Now, there doesn't seem to be much either way. It's more how can you think critically through the specific question you're trying to ask? Right? It's not are these good or bad? It's let's think about a very specific question and then turn to some of the things that you've outlined. Even earlier, when you mentioned that, hey, maybe for older people that have a very high degree of inflammation going on. They have a high oxidative stress burden. Maybe there, we would see if we could target or at least you could make a theoretical case while you would advise it. So just thinking through things a bit more deeply. So I certainly see that as your takeaway as opposed to yeah, none of this matters.

ERIC TREXLER: And one other thing you asked about whole food interventions, I know that there is at least one intervention out there, where they basically took people and said, hey, try to get more nitrates in your diet from foods, no supplementation, and they did find a very positive effect of that. And so that's something to keep in mind. Like along with your question. Was that a nitrate intervention? Yes. But did those people almost certainly increased their antioxidant intake? The answer is definitely yes. And so I think the focus on building a well-rounded diet should really be a take home point of especially like you said, people who have potentially a high oxidative stress burden, really focusing in on making sure that

we've got ample antioxidants in the diet, but we don't need to do that with supplementation. We can find that in food and along with those antioxidants we're seeking, we're bringing in a lot of other potentially beneficial phytonutrients

DANNY LENNON: Right. And actually, from a pragmatic perspective for nutrition practitioners listening one thing I tend to talk about is, this can be a way to smuggle in better nutrition habits to athletes you tend to work with, because rather than just trying to get them to eat better quality food now you can provide this rationale of, oh, I'm not just trying to get you to eat these vegetables. We're trying to increase your nitrate intake, because it has X, Y and Z impact. And so you can use that to your advantage of an overall healthier athlete because their overall food intake is better. And you're using that through this way to smuggle in with some of this literature I guess.

ERIC TREXLER: Definitely. Yeah.

DANNY LENNON: And then also to pull back on your previous point from someone who is incredibly introverted as well, but my writing is probably very inferior to yours. So hopefully I am not that bad at talking. Otherwise, I'd kind of be screwed if I was, but.

ERIC TREXLER: I am just confirming my own biases. Like I said it was the least evidence based –

DANNY LENNON: So you're doing pretty good. People like to hear you talk. So.

ERIC TREXLER: I appreciate that.

DANNY LENNON: Yeah. And speaking of that, where can people find you on the internet?

ERIC TREXLER: You can find me on Instagram at TrexlerFitness. You can also find me at StrongerByScience.com. We've got articles. We've got podcast. And you can also find me in MASS, that is our monthly research review that goes out the first of every month. We have 10 pieces of content every month looking at recent research, and the authors are me, Greg Nuckols, Dr. Eric Helms and Dr. Mike Zourdos.

DANNY LENNON: Amazing. And so with that, let me leave you with the final question around the podcast out on. You may have got it before but I do not remember what your answer was. So and I'm sure –

ERIC TREXLER: It's changed...

DANNY LENNON: Oh, I'm sure mine would change on a weekly basis, never mind over a span of a few years. So if I were to ask you, if you could advise people to do one thing each day that would have a positive impact on their life what would that one thing be?

ERIC TREXLER: You got to sleep Danny. You got to sleep. Honestly, the biggest impact, especially in the last year in the last 18 months or so I transitioned from being a doctoral student in a research lab with human subjects set schedule, wake up everyday get to the lab early. Now I'm an internet person. I work from home. No one, I'd have nothing to wake up for in the morning. That sounds worse than that's not what I mean. By but no one's telling me hey, Eric, you got to be up at 7am. My sleep habits the first several months just absolutely deteriorated. Nothing makes you feel worse. And you can trick yourself into thinking it's something else. But please prioritize really good sleep habits. There's just a million benefits and no downsides.

DANNY LENNON: I love it. And it definitely confirms my bias of rambling on about sleep a lot. So I'm glad.

ERIC TREXLER: It's so important.

DANNY LENNON: Right. Eric, thank you so much. I really enjoyed this conversation and it was great to talk to you again.

ERIC TREXLER: Yeah, thanks for having me on. Hopefully we'll talk again soon.