

## Stabilize Your Blood Pressure Using Biofeedback – Mackay Rippey with Dave Asprey – #853

Announcer:

Bulletproof Radio, a state of high performance.

Dave Asprey:

You're listening to Bulletproof Radio with Dave Asprey. By the way, this might be one of the last few episodes where I call it Bulletproof Radio. I am contemplating a name change and I'm pretty excited to share what it's going to be with you when it comes out. In the mean time, definitely Bulletproof Radio.

Today, we have a live studio audience, actually one of the biggest ones we've ever had coming in from the Upgrade Collective, which is my membership and mentorship group, and if you were able to listen to and see the back conversations that happen in the chat rooms during the podcast, you would love it and you're missing out if you're not in the Upgrade Collective. It's one of the fun things we get to do. So, I'm actually looking at, oh, about two dozen people live and in addition to today's guests and just having a lot of fun with it.

Today's guest, speaking of it, is going to talk about biohacking, blood pressure, and the cardiovascular system. And you might say, "Blood pressure? What do I care about?" Unless someone tells me I have high blood pressure or maybe low blood pressure, then you probably just don't think about it. But it has profound effects on how long you're going to live.

So, I asked Mackay Rippey, who's a medical advisory board member for Zona Health to come on. We're going to talk about nitric oxide, endothelial cells, red blood cells, and blood pressure. And if you're into biohacking or just feeling really good, you might know a thing or two about nitric oxide as, that's what enables erections. That's kind of important but it does all sorts of other stuff throughout the body including in women who typically don't get that kind of erection. And endothelial cells, we talked about on other episodes, these things that line your blood vessels that are terribly important for performing well as well as feeling well.

And it's going to be a fascinating conversation because there's direct feedback. I mentioned that Mackay was a member of the Zona Health Advisory Board. There's an episode with the CEO of Zona Health from a couple years ago. I think I interviewed him at Paleo f(x), and this is a device that I've talked about for about 10 years that, with just crazy results and that a lot of people don't know about yet for specifically training blood pressure. Mackay, welcome to the show.

Mackay Rippey (for Zona):

Thanks, Dave. Super excited to be here.

Dave Asprey:

You're an interesting guy because you're actually trained in acupuncture and you're talking about cardiovascular fitness. What's the connection there?

Mackay Rippey:

Yeah. It was quite the leap and particularly, I was trained as a five-element acupuncturist.

Dave Asprey:

Ah! The old stuff. The traditional way. Very cool. Those five elements people who are actually five elements are pretty legit. Okay.

Mackay Rippey:

Yes. So, I'd studied with Worsley and we hugged trees and walked barefoot and stuff like that. And then, somewhere along the line, ran into Lyme disease in my community up here in Central New York and started to get interested in that.

And at that point, jeez, seven, 10 years ago and I know you've had this so this is an old story for you, but for those who aren't really up to speed on it, Lyme disease was an invisible disease. If you got it and you found the community of people, it was like, "Oh, my god. How come we don't all know about this?"

So, we needed to get the word out, so I started a little podcast and somebody along the line said, "You know what? You need to talk to this man, Bob Miller." Bob Miller's this funny, functional naturopath in Pennsylvania and he started hacking into 23andMe data and correlating it with what he saw with his clients.

So, we started to look at genetics and correlating it with what he saw with his clients. So, he started looking at genetics and how that influenced people's health, way outside the box. He's not a geneticist. He's an electrical engineer that got sick, got interested in functional medicine, that type of story.

So, I interviewed him and he was the first person I had spoken to in my almost 30 years as an acupuncturist. He talked about nutrition in terms of systems, not take this for that.

Dave Asprey:

That's why five elements is so cool.

Mackay Rippey:

Exactly.

Dave Asprey:

Systems biology. Biohackers who are listening, we know that that's so important.

Mackay Rippey:

So, that got my attention, so I started looking into biochemistry from a systems point of view. So, I'm not a biochemist. I'm not a PhD, I'm not a doctor. I'm just somebody who's really, really interested.

And one of the wonderful things about the net, as you know, the literature's out there now. You can read for yourself. And if you go in there with an open mind like you have, like your listeners have, you can learn all kinds of stuff that are off the beaten path. We can save stories about that for later. So, that's how I got into it, through the back door, just by accident.

And then I ended up, I heard Mark Young, who's the CEO of Zona, speak on your podcast, the one you reference. I was like, "Wow! This is really cool." So, I reached out to Mark. We formed a friendship and now we collaborate together.

Dave Asprey:

We should explain what Zona is because, for this conversation to make sense, there are people who've been looking at blood pressure for a long time. It's something that affects kidney function. It affects all kinds of cardiovascular outcomes. You guys have read my books about anti-aging. Now, "Oh, gee. Not getting cardiovascular disease would be a first step. The not dying part of living a long time."

Cardiovascular disease is something that kills more people every single year than even our most popular viruses and it's something that is treatable. And if we were to take a tiny fraction of the \$8 trillion we spent on the current thing, and put it towards cardiovascular disease, maybe with some of the current tech you'll learn about today, we could move the death rate and the suffering rate for people in a very meaningful way. And that's system thinking, how do you do the greater good for the least amount of money.

So, what is the Zona thing? It's a little thing that you squeeze that provides feedback to your blood pressure system, so you suddenly get conscious control and you train your body to change your blood pressure and it's a feedback device, and it's not something you get from sticking needles in you with acupuncture, although that can help with blood pressure, it's not something you get from just paying attention. It's something you get from getting a signal that is invisible otherwise.

So, that's what we're talking about here is a relatively simple technology but with computers and feedback and all that kind of stuff and magic happens. You couldn't do this 30 years ago because the tech couldn't exist but now it does. Good description, bad description?

Mackay Rippey:

I think it's a great description. The tech was there 40, 50 years ago, but it was in fighter technology tech and spending millions of dollars trying to keep pilot from passing out while they're pulling negative Gs. So you couldn't have that. And now we've got things like the blood ox sensors that are, what, 15 bucks you can buy at Walmart.

And so this isn't quite a \$15 device but you can get this device in your own home and use it to ... And I'm embarrassed. I should have mine in front of me. Mine's is downstairs by my coffee pot where I make my Bulletproof Coffee, by the way.

Dave Asprey:

I should probably ... I think I have mine on the shelf over there.

Mackay Rippey:

Anyway, so I can't show people. Mark's going to kill me but sorry, Mark.

Dave Asprey:

And, I mean, it looks like a joystick from a fighter airplane with a little digital screen on top. And most people are listening to this anyway. And the idea here is that, okay, we could say, "I'm going to look at your salt consumption." By the way, current recommendations for salt are so low that they're increasing your risk of heart attack and that is quantifiable.

So, you could say, "Let's look at that. We're going to look at ways to change kidney function," so some way to modulate your blood pressure using usually drugs or they're going to tell you to restrict the salt and exercise a whole bunch and all sorts of things that are kind of systems based. But the approach from Zona is what if we just looked at the output of the system without knowing why it's going to go up or down? And we look at, is it high or is it low? What can we do to change it?

And it turns out that that one observation that, "Hmm. When fighter pilots need to control their blood pressure when they're about to pass out, they squeeze really hard." "Oh, does squeezing change blood pressure? So, what would happen if we could play with it?" And I actually don't know. I don't remember or I didn't ask Mark who had that genius idea to say, "Oh, if that works, let's see what happens for blood pressure in people who have it too high." Do you know?

Mackay Rippey:

His name? No, and it's not in my notes. He was the physician working with that. I could look. It's on Jonah's website.

Dave Asprey:

Yeah. It's shared. It was a while ago but it's that kind of thinking. Oh, it's a black box. We don't know what's going on in there. We just know if you do this, this works.

Mackay Rippey:

He played around with it, did all kinds of experiments. But what really got his attention, there were a couple of the fighter pilots in the study who had mildly elevated blood pressure and, for a fighter pilot, that grounds you. You're done with the blood pressure. So, what they found during this study was their blood pressure normalized and that's really what got this physician's attention and the impetus for him to go on and study what this grip was doing. Submaximal hand grip, if you look through the literature, that's the official name for what Zona does. We just like to say it's isometric exercise. It's easier to understand.

Dave Asprey:

When we're looking at maximum exertion, you can have little devices like this, like, "Okay. I'm going to squeeze the crap out of it." And these are professional grade strength trainers for your grip, but that's not what's happening with Zona at all. It's like if you were to just squeeze it a little bit, but not too little and not too much. This weird Goldilocks zone. And when that happens, the normalization is super important. Otherwise, you can look at the set of technologies that we got out of the space program, out of the fighter pilot program.

You guys go to Upgrade Labs and you look at the clinical compression pants that we use there that are inflatable. They're different than what most places who've had kind of copied labs used. And then, ours actually have 16 chambers and work with lymphatic drainage in a different way but they're squeezing the legs.

Well, we learned that from the same research that came out and eventually created Zona, in that we're able to regulate this pressure in extreme circumstances, but now you're not in extreme circumstance. You're sitting on your couch and you're squeezing this thing and it works the same way, which is just kind of cool.

Mackay Rippey:

Now, let's just jump right into some of the biochemistry that I found kind of looking into Zona. So, I started with the hand grip. So, 30% is the magic Goldilocks percentage for your grip. So, you need to calculate what your grip strength is that morning. It can vary from day to day and the optimal is 30%.

Now, if you think you can calculate 30% just by knowing what you're feeling, you're sadly mistaken. That's why it helps to have a biofeedback device that tells you, "You're at 30%. Oh, and, by the way, you have to hold it for two minutes." So, if you think you can do that for two minutes, you need a feedback device. It just makes you life a lot easier.

Dave Asprey:

I don't think you could do this. I'm pretty good with feedback. I run a neuroscience team and this is outside even a meditation master, Bruce Lee kind of guy I don't think could know whether he was at 30

or 50% of his maximum grip strength for two minutes. This is physiologically impossible without a thing telling you what's going on.

Mackay Rippey:

And that's what Zona does. And then, what we've discovered is that the contraction of the muscles open up potassium channels. So, one of the ... You mentioned salt. Let's just pause here for a second for salt. The whole low salt thing. I had a woman come in once. Actually her family brought her in. She's starting to have dementia. "Is there anything acupuncture can do?"

So, I started asking her questions and she said, "Yeah. I'm on a really low salt diet." "Oh, really. How low?" "Well, I've taken all the salt out of my diet. My doctor said to cut back on the salt so I figured I'd go all the way." And I told her, "Tell you what. Eat a little bit of salt." I said, "Don't go crazy. Just put some salt back in your diet and come see me next week." She came back next week and her mind was fine.

So, some of the researchers think that the sodium issue that we're talking about with blood pressure is really potassium deficiency. It's a ratio just like the calcium/magnesium ratio, the potassium/sodium ratio. So, if you have a high salt diet, which no doubt we have a high salt diet. You need even higher potassium which is really tough to do especially when the government says you can only make a pill of 99 milligrams. If your daily intake needs to be 4,700 milligrams, that's a lot of little tiny pills you have to take every day.

And then, the reason they're regulated, it is for safety issues. There's a legit issue with that. You don't want to cause some heart disease problems, some heart attack problems with that.

Dave Asprey:

Well, let's talk about that for just a sec. If you are one of the small percentage of people who can get arrhythmia from normal amounts of potassium, taking a potassium pill, that could cause a problem. Unfortunately, instead of putting a clear warning label on it, they restrict the size. Now, if you were to take, say, Tylenol, which causes 40,000 cases of liver damage or more every single year and treat it with the same degree of caution, you'd have to take 40 Tylenol to get any pain killer effect. So, I don't understand why they're penalizing this.

What I do, and I want listeners to know this, is I take a potassium in a powdered form but not potassium chloride, which is really strong. I take potassium bicarbonate, which is basically like a form of baking soda, and that has other benefits as well so I am getting my four grams a day. Most people don't get it. What happens if they don't get enough potassium, whether or not they're getting enough sodium?

Mackay Rippey:

Well, particularly focusing on these endothelial cells that you mentioned earlier and endothelial just means inside. They line blood vessels. They line lymph, so if you have lymph drainage problems, you might be having a nitric oxide endothelial issue. So, any tube in the body has endothelial cells.

And particularly in the cardiovascular system, they're really functioning as a barrier and a sensor. They're sensing cells. And one of the first things that starts to go in the very, very early stages of cardiovascular disease is these endothelial cells flatten out and one of the main functions of this endothelial cell, one of the ways it senses the need to increase relaxation, vasodilation, but more blood through or oxygen into the tissue is through shear stress. So, that just means pressure.

So, these cells, it's an amazing feat of engineering. They physically sense the rising blood pressure and they trigger through a series of chemical reactions, the release of nitric oxide, which through a series of chemical reactions, tell the smooth muscles to open up and let more blood through the area. If these endothelial cells have shrunk down because of a lack of potassium, they can't not sense the rise in blood pressure and the demand, so you end up with mild hypoxia in the beginning that gets worse and worse and worse.

Dave Asprey:

Wow. It's one of the reasons I eat a lot of butter because it lubricates my endothelial cells so they'll be safe.

Mackay Rippey:

Potassium replumps up ... No. I don't mean to go on there. I wanted to go back to the potassium.

Dave Asprey:

Potassium is the thing. It's not the butter, but that's an old meme.

Mackay Rippey:

Oh, is it?

Dave Asprey:

But people always ... They agree with the fats.

Mackay Rippey:

I eat butter all the time. I know. I eat butter all the time.

Dave Asprey:

Yeah. So, you don't have to worry about the butter but butter isn't going to fix that problem. It's a mineral issue and it's a potassium issue. But there are still people who say, "Oh, I got the memo. Salt is important for life and resilience in stress management, but I don't want to be low in potassium, so I'm going to supplement my potassium. Now, I've got enough sodium. I've got enough potassium." By the way, for me, it's about six grams and sometimes eight grams, if I'm working out or doing something more strenuous, of salt. I use Himalayan salt or Redmond salt. But that's what it takes for me to have enough blood pressure that I don't get brain fog. This is not abnormal, so four, five grams of salt. If you're not retaining water, cool, but you also need potassium to balance it out. The ratio of the two matters.

But even if you're doing that and you have high blood pressure, there are some things. Diseases of aging, cardiovascular disease, calcium plaques, chronic stress, pre-diabetes, which 60% of people have but probably not 60% of the Upgrade Collective. If you have kidney disease, you can have toxins. All these things do it. You can just have a really mean mother-in-law. So, no matter the cause, if you're doing a biofeedback-based training like Zona, does it work the same for all of those?

Mackay Rippey:

I'd like to say, "Unequivocally yes." However-

Dave Asprey:

There may not be studies for each of this stuff, because we don't know the cause for a lot of people.

Mackay Rippey:

That's my hesitancy is to put a flag down and say, "Absolutely," and then have some government agency with black helicopters come by and say, "You guys are lying about what Zona can do."

Dave Asprey:

Oh, they have a whole spectrum of colors of helicopters. It's totally different now.

Mackay Rippey:

We got rainbow helicopters now?

Dave Asprey:

There's some green ones. There's some blue ones.

Mackay Rippey:

That's awesome. It's about time they diversified.

Dave Asprey:

Now, okay, so we don't know but we know that it works and since most people they don't have one cause anyway. They have a mix of those causes. Slightly depressed kidney function, et cetera, et cetera, but we know that when people show that symptom, regardless of the cause, they're doing feedback training and they're getting results. What percentage of people lower their blood pressure back to normal by using Zona?

Mackay Rippey:

It's about 80%.

Dave Asprey:

Yeah. It's above 80%. So, guys, this is why it's worth an episode. Zero drugs, zero changing in their diet and supplements, zero changing in their exercise, all of which are good things to do anyway except for maybe the drugs.

What happens? Wow! Who would have thought? But 80%. If you wanted to reduce the death rate to, oh, I don't know, say 600,000 lives a year, lowering blood pressure. I don't know. Would we hit that number? Probably. Looking at deaths from cardiovascular disease, including stroke, heart attack, and the associated causes, it's in line with that but probably not quite as high as that. Of course, it would reduce susceptibility to other things as well, but that's a whole other question.

Mackay Rippey:

Yeah. That's the thing. So, one of the issues. I don't know if you get that with your members in your group, but my patients, who are fairly educated, come in and, "How's your blood pressure?" "Oh, it's okay." Then, you ask them what drugs they're on and they're on three or four blood pressure

medications. "What. I thought you said your blood pressure was okay." They say, "Oh, yeah. But it's under control."

Dave Asprey:

That is the biggest bunch of garbage. It makes me mad.

Mackay Rippey:

Isn't it?

Dave Asprey:

The number of people with dementia, brain fog, or even senile cognitive dementia, which is pre-Alzheimer's, those diagnose. You take them off blood pressure medications, they get oxygen in their brain and they don't have dementia. It is nuts. You go to a retirement home or an assisted living facility and half the people there are on blood pressure medication that's causing them to be in a stupor. It's important to have enough blood pressure, and the drugs that do that are oftentimes really not good for you and you don't want to go there. You do want to go there if you can't go to another way, because you'll destroy your kidneys if you don't, but maybe the other way would be, "Hey, I'm going to train my body by doing eight minutes of day of squeezing little things while I do something else." It's pretty ...

Mackay Rippey:

That's crazy talk, babe. Crazy talk.

Dave Asprey:

Yeah. I don't know. Maybe. I should retire as a biohacker and go to work for CNN.

Mackay Rippey:

Cheers.

Dave Asprey:

There's a question here from one of our Upgrade Collective members about if you're normotensive, in other words, you have normal blood pressure or maybe slightly low, is it useful?

Mackay Rippey:

First of all, one of the things we found that was interesting was the Zona device, we didn't expect this, normalizes blood pressure. So, if things are a little bit low, it can help raise it into a more functional range. Now, again, we can't say that officially but that's something that we have noticed anecdotally from people's reports.

Dave Asprey:

You're allowed to talk about clinical results and just you have to put the asterisk in there. And it's funny. There is no law or even rationale way of thinking that says only double blind clinical trials are valid. There's seven forms of evidence and observation in the clinic is actually oftentimes the most useful. And that is where most medicine was founded were Chinese medicine, Ayurveda, a few things that are proven to work.

So, just for listeners, that's important. But you're saying it does raise blood pressure if you have low blood pressure. I didn't find that. So, I have low blood pressure. I probably have a genetic thing. I've had low blood pressure my whole life and you can say, "Oh, look at you." No. Low blood pressure is worse than high blood pressure if you don't want to pass out a lot and you want to have a brain that can focus.

So, I'd know how to keep my blood pressure high. That includes eating enough salt on my food. But, when I did the Zona for a while to see if I could raise it, I didn't notice a difference in it. But it could be because of a cause of mine being genetic versus epigenetic or lifestyle, right?

Mackay Rippey:

I would think so. I'd think if we could dive in and look at your endothelial cells that they're functioning pretty well and there wasn't a whole lot of gain there to recover from. So, that's what I would say.

Dave Asprey:

How important is our nitric oxide system to this because you mentioned nitric oxide with the Zona, but there's three kinds of nitric oxide. I tend to make the bad inflammatory kind instead of the endothelial kind and do you know is there a genetic thing that says whether Zona's going to work better or work less on a nitric oxide system?

Mackay Rippey:

How long do you have? The nitric oxide is the molecule that ties this all together and it's an amazing molecule in that it's dose dependent, so small amounts. You talk about the endothelial cells making endothelial nitric oxide and there's neuronal nitric oxide and these enzymes put out just tiny little puffs of nitric oxide that keep the cells humming, that keeps your brain humming, that keeps your muscles humming, that keeps your sex life humming. All that working together there.

Then, there's the inducible nitric oxide and that releases nitric oxide about a thousandfold increase. And that's the whole cytokine storm that we're talking about, that whole death by sepsis. That's all these horrible reactions that the body has to an infection or an invasion and the body ends up killing itself because it can't regulate it. That's what happens when the inducible nitric oxide gets out of control.

Dave Asprey:

So, you don't want to take beet root if you're dealing with iNOS, inducible nitric oxide, right?

Mackay Rippey:

Yeah. Probably not and then also, there's a whole oxalate thing. So, I don't know if you've gotten into that in any of your episodes.

Dave Asprey:

Quite a lot.

Mackay Rippey:

But oxalates are kiss of death for a lot of people, and so beet root isn't maybe the thing. If you want to get some nitrates in your diet, endive is a great source of without the oxalates in it.

Dave Asprey:

I mean, endive will make you fart like no one's business.

Mackay Rippey:

I have it. I have that problem.

Dave Asprey:

I would say probably has a lot of fermentable carbohydrates in it. You might do well with a beet root extract, which shouldn't have a lot of oxalic acid in it but people are saying, "I'm going to eat big buckets full of beets." If you have the right gut bacteria, you'll be all right, but oxalates can increase inducible nitric oxide. I find that that happens in my case, so I'm kale's biggest enemy. They're trying to kale me.

Mackay Rippey:

Yes. I'm working with a company. If I tell you we're coming up with something called Kale Buster. We're trying to just kill of kale as a food. It'd be cows and pigs maybe, but people, no.

Dave Asprey:

My pigs kind of spit it out. They'll eat a little bit of it, but even the pigs are not fans of it. They'll eat the cabbage before they eat the kale. Yeah.

Oh, here's a question from John. "Is Zona going to help with POTS, postural orthostatic hypertension?" Now, you treat Lyme clinically, which in my mind is largely toxic mold media, like toxic mold causes Lyme to go out of control. So, in both Lyme and toxic mold creates that low blood pressure. You stand up, you pass out kind of thing and Nick Foles was on the show. We talked about his wife, Tory, and how she'd been dealing with that.

So, talk about blood pressure, nitric oxide, Zona, health, and orthostatic hypertension. What's your take on that?

Mackay Rippey:

Well, your blood pressure ... I mean, that's one of the problems with controlling blood pressure is there's so many inputs to it. And if it's a vagal nerve brain function issue where, or the sensor for the brain that's in the ... And I forget what it's called, but the brain has its own blood pressure sensor in your neck and if that's not functioning properly and that's a lot more related, connected to the brain than your individual endothelial cells are. So, there's a dysregulation there. Enhancing your overall endothelial health will be good for you but it probably isn't going to cure the POTS. Does that make sense?

Dave Asprey:

It makes a ton of sense. Now, if you have a control mechanism problem versus a functioning of the blood vessels themselves problem, so where Zona's going to help is the blood vessels can work really well, but if they get no signal to increase blood pressure when you stand up, you're still going to have a problem. You guys sort of see the difference in the Upgrade Collective here? Why one is a signaling problem and the other is a systems problem and Zona's looking at the systems problem and you would use vagal nerve stimulation techniques to deal with the signaling problem, which seems to work very well. Or maybe acupuncture. Can you stick needles in the vagal nerves and flick them a few times to make people wake up?

Mackay Rippey:

Some points in the back of the ear to increase blood pressure and then, right, it's all yin and yang, so if you got too much yin, blood pressure's going to be down so you need a little more yang in your life.

Dave Asprey:

That's my problem. I'm so yin.

Mackay Rippey:

Totally.

Dave Asprey:

By the way, if you're not familiar with acupuncture, yin is the feminine energy and yang is the masculine energy. So, I was calling myself girly, which is totally fine.

All right. Let's talk about hypoxia. What is the relationship between blood pressure and hypoxia?

Mackay Rippey:

There are two issues with it. Obviously, if you have hardening of the arteries, if your blood vessels aren't expanding too loud, the red blood cells through to release their oxygen, the tissue is not going to be fully oxygenated and that's what hypoxia is, low oxygen.

Now, just because you have oxygen in your blood and that's gets measured with the little finger device we all have now, because of COVID. Can we say COVID on this show or do we have to say that which must not be named?

Dave Asprey:

Yeah. It's a new dessert topping. It's okay. We were talking about that definition, not the other one.

Mackay Rippey:

Excellent. Just because it's in your blood doesn't mean it's getting to the tissue, which is a big issue and that's one of the big problems I think with all these blood pressure medications. And you're talking about, too. They weren't. The biggest side effect for all the blood pressure medications are lightheadedness and passing out. Gee. Why is that happening? Hmm. That's because your brain doesn't have enough oxygen. Oxygen's kind of important for brain functioning, especially as we exit our 30s, let's say.

Dave Asprey:

It's really important that people understand that thing about blood pressure in the brain. Years ago, when I was going to Wharton business school, Ivy League kind of thing, I was about to fail out and I went and I got one of Dr. Daniel Amen's spec scans, right when he'd first written his book, before he had the level of respect and understanding he does now, and they found all kinds of brain problems but including low blood flow in the brain. So, I didn't understand the nature of having low blood pressure in addition to all the other crap I had, a history of Lyme and mold and toxic metals and all kinds of stuff I talked about on the show before.

But interestingly, he did find that when I came back after doing all this biohacking, all this stuff that I've been writing about, that my blood flow in the brain was noticeably improved and I take herbs

every day that are documented to increase blood flow in the brain and even standing on your head and whole body vibration, all kinds of stuff you can do, but it's about getting enough oxygen to have enough electrons in the brain, because no matter how many ketones you have, no matter how many smart drugs you have, if you don't have the raw fuel, your brain won't work well.

And so, what you're finding is that this is a problem in the brain. When people use the Zona, they're training their endothelium basically to be better because it normalizes blood pressure, that they're seeing better cognitive function.

Mackay Rippey:

It's normal for your blood pressure to go up, to go down. It's normal for the demand of the tissue to go up and down in terms of if your liver's dealing with mold toxicity, it's going to need more oxygen. If you're working on, I don't know, studying something, your brain needs more oxygen to work. If you're working out, your muscles need more oxygen.

So, your body needs to be able to adapt. It's designed as an adaptive system and the main signal for that adaption in terms of getting oxygen and other nutrients in, talking about the ketones, the other nutrients to the individual cells. And then, the toxins back out again are these endothelial cells. And they're the sensors that open and close the valves, your blood vessels that control how much ... You don't want too much oxygen. That causes too much oxidative stress and you don't want too little, because then your mitochondria aren't getting enough oxygen and then they start creating all kinds of reactive oxygen species.

So, you actually start ... That's the start of a lot of the disease process, but it happens so suddenly, so slowly, over so much period of time, that's why something like the Zona's so important. You don't need it now. Now's the time ... When do you start exercising? When do you start using your brain? Now, before you've lost your muscle tone in your 60s or 70s and you're trying to recover it back and it's much more difficult. So, now's the time to start "Exercising," quote, unquote, your endothelial cells so that they continue to function well as you increase your age so you're not only living longer, but you're living well as well.

Dave Asprey:

This is a new question just occurred to me, but when you look at high impact exercise which is not very good for you if you want to live to at least 180 like I do because you won't have all of your joints if you do this for a hundred plus years. But is that high impact as one of the benefits and there are some benefits like exercise in addition to bone density from piezoelectric effects on the bone matrix.

What about blood vessels? Is it actually creating a surge every time you land on the trampoline or every time you hit the ground hard? Is it probably doing something beneficial to the endothelium? I bet it is.

Mackay Rippey:

I have not seen those studies. That's a fascinating question. Heat, right? Heat shock proteins affect this. Obviously the shear stress we're talking about, vibration, UVA rays all affect us. So, I would not be surprised if something, a shock like that would be sending a signal to, hey, we need some more blood here.

Dave Asprey:

All right. That is fascinating. That's cool. I hadn't thought of that, either. There's something else that I don't think I've ever talked about it on the show but it's something that I really experienced when I was living with mold and recovering from it and it's exercise intolerance. And people are saying, "Oh, you're just lazy." And they said that to me when I was fat, too. And I will sit on you right now.

So, what happens with exercise intolerance is you're saying, "All right. I want to exercise. I'll go for a hike or I'll go lift weights or something," but then you feel like crap for four or five days. You can't even get out of bed. You're so tired and it's not about weakness. It's just like you do it. It's reliable and repeatable, that you know you're going to feel that way. So of course, why would you exercise? And some of the people in the Upgrade Collective are like, "Oh, yeah. I know about that."

And there was a time when I'm like, "I'm just going to do it anyway." And eventually, I probably got out of the mold and just kind of pushed through, but it was miserable and I'm surprised I kept my job. I mean, I don't even know how I could focus on anything. What is going on when you have exercise intolerance and what is the role of blood pressure in it?

Mackay Rippey:

Normally, when we think of exercise intolerance, unfortunately, you mentioned a lot of it is, "Oh, you're just lazy. You've lost your will power. You've become a weak person." Which is just utter B.S. It just, it's physiological. It's not a mental problem. It's not a will power problem. It's a physiological problem, and a lot of time in the functional medicine community, we talk about adrenal fatigue. "Oh, you don't have enough adrenaline and we just need to goose you a little bit."

But, as you know, when you're in that state, you can get an adrenaline surge and get something done and then, what the people with the chronic fatigue and few spoons, they call them spoons, have to give is you pay for it for the next, what? Day, two days, three days, a week.

So, it's not simply the adrenaline surge, because if that were the case, yeah, you'd just be sleepy for a couple hours. Then, you'd be kind of back to whatever normal was. There's some researchers who are thinking that one of the things going on, maybe the thing going on is, again, hypoxia. We're back to that word again, that your tissues aren't getting enough energy and, as a result, your body's shutting down to protect them. Again, we've mentioned very briefly with the electron transport chain inside the mitochondria, if there's not enough oxygen there, instead of creating ATP and energy, it's creating oxidants. You're rusting from the inside out. You're burning yourself from the inside out.

So, as your mitochondria get further damaged, you have less energy. As you have less energy, you less energy to do things. And it's just this downward cycle into despair. A lot of people, especially with Lyme disease, talk about just at some point, "I can't go on anymore like this. I just want my life back." It's brutal and that's where the proper blood pressure, that's where the proper blood flow, that's where the proper endothelial function comes in. That's where nitric oxide comes in, to open up these blood vessels to send those signals out.

So, we, again, thinking in terms of systems, the doctors who think in terms of systems have such an advantage, the researchers, rather than, "Okay, the person's maybe just ... They can't get their heart rate up, like an athlete who's overtraining. They can't get their heart rate up. They'll come in and tell me, 'Yeah. I just could get up above 120 today.' It's like, 'Well, rest a little bit.'" And they know they're overtraining, too, but, "Oh, well, we just need to get your heart rate up." Maybe it's the tissues, the end, the sucking of the oxygen into the tissues that the issue is here.

Again, and then we follow it all the way back. We've got the oxygen, the platelets themselves. You think about, a platelet has to squeeze through a microtubule to get to where it needs to go. It has to deform. So, these platelets, the red blood ... Sorry. Red blood cells, I mean red blood cells, not platelets

are releasing nitric oxide to help expand that little tiny blood vessel that they're trying to squeeze through.

So, this nitric oxide is the whole thing and as long as there's a vessel, they're all endothelial cells there. They're endothelial cells and they get that signal and if they're not properly functioning, they don't expand. So, that red blood cell can't make that last the 8%, .8%, whatever of the journey is to release the oxygen where it needs to go. And so you get this hypoxic tissue that starts to build up.

And as you know, I'm sure I've heard this on your podcast a hundred times if not a thousand times about the source of cancer and hypoxia and, as opposed to, well, it's a genetic mutation. Well, why did the genes mutate? Well, because the cells were starving from oxygen.

So, if you don't have proper blood flow and oxygenation, you're either going to get heart disease or you're going to get cancer, case closed. Unless you get run over by a bus and that, just don't play in the street.

Dave Asprey:

The idea of pseudohypoxia is really interesting. We're talking about that on this week's Upgrade Collective call right before this and pseudohypoxia is when you have enough blood oxygen but your tissues are hypoxic. So, you technically, in a hospital with a thing on your finger, they're looking. "Oh, your SpO2 in normal. It can't be that. I wonder why you're going into sepsis." And then, if you're still coherent and you're the patient, you say, "I wonder why you haven't seen all the studies on PubMed talking about how almost any mitochondrial stimulating natural compound, all of them, whether they're herbal or nutritional or amino acid, all of them show efficacy against sepsis."

And you wonder why guys like Paul Allen die of sepsis, from bad care because doctors know that the more successful and more public you are, the less they can do what works and the more they have to follow the standard of care so they don't get sued by your billionaire relatives. So, moral of this story is have good friends as doctors if you're famous.

Mackay Rippey:

Sad but true.

Dave Asprey:

Sad but true. So, we know that fixing mitochondria fixes sepsis and that pseudohypoxia is a problem. How many people do you think get pseudohypoxia when they eat kale?

Mackay Rippey:

All of them.

Dave Asprey:

All of them, because of the oxalic acid connection, right?

Mackay Rippey:

Probably, yeah. I mean, that's-

Dave Asprey:

I will tell you, I eat kale, I eat raw spinach, other high oxalic acid foods, even an overdose of blueberries, which are in season right now in BC, which is relatively high in oxalic acid. You know they're good for your brain. And, for me, it's always been along my spine. The muscles there, the erector spinae, they will cramp up when I get too much oxalic acid. It's a very clear indicator for me. And if I eat three or four cooked beets, it's game over. I'm going to be in pain. And some people handle it better. There's a gut bacteria connection. There's probably some genetic stuff. There's some salvation things.

But if I was to go back and say, "All right. I'm going to train my endothelium to be more resilient, is that really going to help me with that problem or is that independent because it's just pseudohypoxia caused by chemicals? Don't expose yourself to the chemicals, even if your endothelium works.

Mackay Rippey:

I think at some point, one of my friends, Emily Givler likes to say, "We live in a toxic soup of a planet." As some point, we're overwhelmed. We're swimming uphill, upstream through this toxic soup. So, the less we expose ourselves, the better. And the better our system is, the better it can respond to damages and stress, the better we'll be able to deal with that.

Now, and we got to remember, oxalate your binding with minerals so are you mineral, right? Are they depleting magnesium from you? Is it the actual tiny little evil shards that they form, crystallizing in your spine there? What exactly is going on with the oxalate? There's so much that can happen. So, who knows?

But in order to heal from it, you definitely need to be able to get the blood flow moving through that area and if it doesn't respond properly, it's not going to happen. That's one of the problems with injuries. Talk about with Lyme disease. Lyme disease finds your old injuries and whenever we have damage there, that's going to be a potentially hypoxic area, just because of how things remodel. And the body does it's best to make new blood vessels but the ones you were born with are the best ones.

Dave Asprey:

I don't know. Is that really true? I've seen, even going back, like Julian Whitaker, one of the very old and the first guys to say, "Guys, even with heart attacks, you can grow new blood vessels around any clog, any times there's new tissue, we're always worried about growing new blood vessels because ... Oh, cancer might use it even though it seems like that's part of our repair." Are those new blood vessels inherently weaker than the original ones?

Mackay Rippey:

They're not inherently weaker. They're just not going to be as efficient and they're taking the slow road around. It's like around here, we've got the thruway. When the thruway backs up, you can old Route 5 to get to Syracuse but it's going to take longer. You got to go though Chittenango and all the other little towns.

So, that's all. So, yeah. I mean, that keeps a lot of people alive and, again, that's part of the nitric oxide signal. If you don't have enough nitric oxide signaling from endothelial dysfunction, the body's not going to get the signal. It's not only do we need to open up. If then the body fails to open up the blood vessels, it's the next step is, "Oh, we better grow some new blood vessels." So, they're both come out of the same signaling pathway, I would argue.

Dave Asprey:

Okay. That makes some sense. I'm thinking about maybe I had to use my Zona because I noticed it didn't raise my blood pressure. I don't have high blood pressure. It's one of those things like, "This is really cool." But it's the tool for what I don't have, but you're inspiring me to wake up the lining, especially with increased potassium intake.

So, should you take a handful of potassium if you're not sensitive to it and it's not going to cause cardiac problems before you do a Zona thing? And when I say, "Doing it," it's eight minutes of looking at a little thing and squeezing. It's not particularly difficult.

Mackay Rippey:

I don't know what the timing is on the absorption of potassium into your blood stream and I would argue there's two things going on. Your body is not going to let your serum potassium level stay high for too long. It's going to normalize those really quickly. That's what your kidneys are doing. That's what the rest of your cells are doing. It's going to respond.

So, that's one reason why I think Zona works like this and also, it's ... The phenomenon where you do it the first day. "Is my blood pressure lower?" No. Second day. No. Second week, maybe. Fourth week, probably. Sixth week, almost for certain. So, what happens is, we finally get to the tipping point where there's been enough flooding of potassium, short term flooding of potassium in the body, reconditioning the endothelial cells that they finally reach a point where they can begin functioning again.

So, I think taking a supplement of high dose potassium is probably a good idea and may have a similar effect to what the Zona is doing, but again, it's very short lived. So, doing the Zona would give an additional boost where you don't have to take in additional potassium, because at some point, you don't need any more potassium. Again, you talk about the danger of it or you're just going to pee it out. So, the Zona is a way to use what you already have on board and get the spike of potassium, get the endothelial cells working again, raised.

There's a great study that has microscopic pictures of the endothelial cells, that shows them flat and then, after potassium, plumped up. It's so cool. So, that's what I would argue there. So, we're dealing with work synergistically, probably. But the timing of it would be how do you time that so that they both hit the cells at the same time? I don't know.

Dave Asprey:

I think once you open the potassium channels in the muscles using the Zona, as long as you have potassium sufficiency or if you take it before, during, or after, my guess is they'll be open for a little while and it would probably work pretty well. You're talking about those pictures of the Zona or of the endothelium. You guys presented or not you guys. You don't work for Zona but you just use it in your practice or you're on the advisory board. The Zona presented at The American Academy of Anti-Aging Medicine where I've had the honor of lecturing quite a few times, and presented that data about flat endothelial cells. And whether you're a pro athlete or you're just looking to live a very long time or anything else, if this is going on, this is an early, you're heading in the direction of disease. And you guys showed pictures and you publish research about how potassium softens the vascular endothelium and increases nitric oxide. So, and the way you're talking about, there was that study, right?

Mackay Rippey:

That's correct, yeah.

Dave Asprey:

Okay. Now, here's my question for you. I want to do my super Zona protocol. So, increasing nitric oxide release. Should I take some L-arginine? It's an amino acid that increases your nitric oxides. I mean, I could take that. Heck, I could pop a Viagra if I really wanted to, not that I have any, but I'm sure I can get a prescription that raises nitric oxide as well. Not suggesting that we all go do that. There are other ways to do it. And I could do some beet root extract, which might also do this as well and I could do red light therapy that increases it, and then I can do my Zona and really spike my potassium and spike my nitric oxide. I know there's no studies in any of this but you have clinical evidence so there's no limitations on what you can do before, during, or after Zona, what's going to be the super crazy biohacker stack.

Mackay Rippey:

How I will stack it. Well, first of all, I'd skip the arginine and take citrulline instead.

Dave Asprey:

I like that answer. I would actually do the same. Wow!

Mackay Rippey:

My understanding is, it just has to do with how it gets to the nitric oxide synthase itself. The liver loves arginine. It needs it for the urea cycle and for the detoxification of ammonia and it primarily gets metabolized and used there before it makes it into your system and the levels actually go up near the cells where you need it, near the endothelial cells and the smooth muscle cells. Citrulline gets taken in, gets moved to the kidney first and then distributed and gets converted through, again, part of this urea cycle in the cells to arginine kind of on site, so it's a just-in-time delivery.

It's just, there's studies showing that it's just a little bit better or maybe a lot better at getting your nitric oxide levels up. So, that's why working with Vitalize Life, we made a citrulline base for the supplement and not arginine. Now, there are good reasons to use arginine, but to boost nitric oxide, not the best. Sorry I went down that rabbit hole there.

Dave Asprey:

No. This is really helpful for listeners because the people listen to this show are the kind of people saying, "How do I get more results in less time?" And I'm saying, "Okay. You've got a Zona," and we already talked about the results.

Mackay Rippey:

Citrulline and some vitamin C. You need to make you get a little bit.

Dave Asprey:

Vitamin C.

Mackay Rippey:

Yeah. You want to make sure you've got your B vitamins, particularly B5 onboard. You need to make sure your NAD is up, your NAD pH particularly. So, that starts it all up by donating electrons, so you got to make sure those pathways are functioning.

So, that, in terms of kind of the supplement side, that's what I would look at. Those would be the main ways to prime the nitric oxide synthases to get ready. Now, there's a thousand other things you could do but those are the low-hanging fruit there. And then, things like your vibration plate,

exercise stuff. Vibration releases it. It's another stress on the system that releases nitric oxide. So, saunas, red light, and infrared, the heat shot protein releases nitric oxide.

So, basically, if you're able to and you talked about this earlier, your inducible nitric oxide. If you can get your inflammation down first, then you're going to be producing maximal amount of nitric oxide. If you're inflamed as well, then it's a little bit dicey on producing the nitric oxide.

So, the more you can do to bring your inflammation down, so that the redox status in the cells are in decent shape, then you're probably going to be producing nitric oxide instead of superoxide and we didn't really talk about that but these nitric oxide synthases can produce superoxide when the cell is stressed. In fact, I think it's one of the main signalings that the cell say, "Hey, we're in trouble here." It no longer produces nitric oxide. It produces superoxide which starts a whole nother chain of oxidative signaling.

Dave Asprey:

And you need some SOD to turn off inflammation but if you make too much SOD, you'll feel like absolute crap. You can take supplements with SOD and I've had issues from too much SOD from those.

Now, I should mention, too, anytime someone comes on the show and we're talking about a product, if I can get a discount worked out for listeners, I do. You go to [zona.com](http://zona.com), Z-O-N-A, go dave2021, save 150 bucks, which is a real meaningful savings. It's not a terribly expensive piece of technology. In fact, I think it costs less than what an annual amount of pharmaceuticals would cost.

Mackay Rippey:

A lot less. Yes.

Dave Asprey:

It lasts a very long time and it's a piece of technology. So, just for listeners who may be tuning in now, I've been a fan of this for 10 years. And one of the first products I mentioned. In biohacking, you can do stuff to the body that you would not even believe is possible. And I think the tech for Zona has so much evidence behind it now that it's pretty shocking, especially when I go look at the global literature outside the US on what's possible with it. I'm like, "Wow!" There's some studies that are published all over the world that says it's pretty cool.

And if, look, if blood pressure and nitric oxide and potassium are not your top priorities right now, hey, don't get the Zona. Maybe you just learned something here that said, "I really, really should take enough potassium." That's a good thing. You're starting out, but if your blood pressure's gone up or it's happening in your parents and all, getting on top of it quickly, using tech, using supplements, using all the stuff we talked about, look, it can save someone's life but more importantly, it can maintain the quality of life because your brain works because it's getting blood, because your muscles work because you don't have pain throughout the body.

So, I look at that endothelium and even the lining of the endothelium, the glycocalyx as primary biohacking territories and the idea that you can use feedback, any system in the body where you can get external feedback will improve more quickly than if you just sit there and try and look at it, even if you're a meditation guru and you sat in a cave and you can make your thumb or your hand get really hot here and there are guys who can do that. They can change 10 degrees body temperature. Hook a thermometer up to it and show them the thermometer and they can do it faster.

So, feedback is just valuable and this is feedback on a system most people know you can measure or have any impact on but it has been around for 10 plus years. And it does compete with chemicals, which is, I think, always a good thing to do.

All right. Would you be up for a question or two from the Upgrade Collective members?

Mackay Rippey:

Would love to.

Dave Asprey:

All right. John's got his hand up but I can't tell if that's because he wanted to ask a question or he just left his hand up. John, since your hand is up, what do you have to say?

John:

Oh, actually the question was really about the POTS because I got a couple of daughters that both get the lightheadedness and we give them salt. They keep salt with them so that they can not stop doing their activities and that raises the blood pressure just enough to eliminate the problem. And when I heard you talking about how you could learn to control blood pressure with this, I thought, "Well, maybe that would work." But I wrote you the question in a text and you really already screened that question, so I don't ... And the POTS is actually originated from Lyme. It's really Lyme-related. The doctor told us it's not actually POTS.

Mackay Rippey:

Right, because it's from Lyme. It's not really POTS. Thank you very much.

John:

Well, she said it is but that most people would treat the POTS and not treat the Lyme. She said it would treat the Lyme and just do the salt for the POTS that the POTS symptoms would improve. And so that's how we approached it.

Mackay Rippey:

How are they doing with their Lyme treatment overall? Are they winning?

John:

No. No. I say they'd improved quite a bit but there's a lot of ups and downs for both of them. Yeah.

Mackay Rippey:

So, then, I'd even turn this over to Dave and his experience but I agree with the doctor in this case. I mean, you obviously need some hacks to get the blood pressure up immediately. I don't know if Zona's the right tool to do that. There's a money-back guarantee. You can try it. It can work. You only need one of them for both your daughters. So, they can try it. If it doesn't work, send it back. And we'd love to hear the results from it.

Dave Asprey:

I should have mentioned that. This is one of those things where ... What is it? 60 or 90 days, some long amount of time. I don't remember what it is. It's on the website. So, guys, don't quote me on that, but you can try it out like, "Oh, look. I did it." You really need to do it for about four or six weeks or something, pretty regularly to start seeing the numbers change. They won't change on the first day. There it's 90 days. So, you can try it for two months and say, "Okay. I got the results. I can see it on my blood pressure," or, "I didn't," and then send it back.

So, I just think that's the biggest vote you can have of confidence when 90 days is plenty of time to see the results and so it's like either it's going to work or it's not going to work. And for specific cases of Lyme, some Lyme co-infections, things like Bartonella will infect the endothelium. In fact, there's a chronic number of people, probably tens of millions in the US alone who have stuff living in their endotheliums, slow-growing bacteria and it's certainly something I've dealt with before. Does doing this kind of training with Zona, where you're training the endothelium, does it affect the co-infections that come with Lyme?

Mackay Rippey:

I have no idea.

Dave Asprey:

No idea? But you treat Lyme and you use Zona. I mean, who else is going to have an idea? You must have an idea. You don't have a clinical study but you have an idea.

Mackay Rippey:

So, again, so we're dealing with ... So, there is inducible nitric oxide synthases inside the endothelium. So, if there's an infection, they are producing crazy amounts of nitric oxide. That does dysregulate the normal functioning of the endothelial cells and the normal functioning of the endothelium nitric oxide synthases.

So, essentially, you're releasing gobs and gobs and gobs and gobs of nitric oxide to try and get the immune system working so it kills off the invader. And so the rest of the nitric oxide synthases says, "Well, we're going to take the day off because we got plenty of nitric oxide here." So, it downregulates the normal functioning there.

So, I would think that if, once the body got on top of the infection a little bit and the iNOS got downregulated, that the Zona would help restore normal function there. But if it's an active infection with inflammation going on there, who knows but in terms of recovery, absolutely.

Dave Asprey:

Okay. That's a very, very cool answer. We have one more question from the Upgrade Collective today. Susan, go for it.

Susan:

Hello. And thank you for this wide-ranging, very interesting conversation about a lot of different cardio benefits. My question is around the actual use of it. So, do you switch hands, stand up, sit down? What are the best ways or the optimum ways to get results and where do you find people making mistakes that we would want to pay attention to if we're going to start this routine?

Mackay Rippey:

Great question. The only mistake you can make is not doing it. It really, it walks you through. So, it's a little handheld device. It walks you through the exercise. As long as you are using the feedback and either it tells you to squeeze less or squeeze more. It's that simple. And then, at the end, it gives you a score about during those two minutes, what percentage were you in the proper zone. And as long as you're above 70% for the entire exercise, you're okay.

So, you can't mess this one up. This is as simple as it gets. You just have to get started and squeeze and takes about 11 minutes, I think, total because there's a one-minute pause in between. You go back and forth two times, but it's as simple as you can get. You literally cannot mess it up. Doesn't matter if you've got the grip strength of Dave Asprey or you've got carpal tunnel and can't squeeze very hard. It's all calibrated to what you're able to do. So, you don't have to be the Hulk to make this work, either. It's not about how hard you can squeeze. That's not it. It's about the maintenance of the tension and the muscles to open up those potassium channels.

Dave Asprey:

The biggest mistake that I've made learning to use the Zona is it's really only two two-minute sessions per hand. So, two in the right hand, two in the left hand. And during those two-minute sessions, you kind of have to watch it and pay attention. So, if I'm saying, "Oh, I'm going to watch Netflix and do this," it doesn't work.

So, the mistake was not paying attention but if you pay a small amount of attention. It's just you either squeeze less or squeeze more but it changes rapidly because you think you're squeezing the same amount but you're not. You're fluctuating all over the place, just like when we tell you to stand still. You're actually wobbling in a circle. You just can't tell and your grip is doing the same thing. You're just becoming better at that fine grain control.

So, it does require attention. So, that means for eight minutes, you can't watch Netflix or do Instagram. But okay. I think most people can handle that.

And, guys, code `dave2021` at [zona.com](http://zona.com) saves you 150 bucks and there's a 90-day money-back guarantee. So, if it works and your blood pressure goes down, keep it. If it doesn't work, then send it back. So, this is one of those things where I'm confident it works because I've seen it work for 10 years.

On that note, we've had a couple questions from the Upgrade Collective. We've learned a lot about nitric oxide, potassium, the endothelium versus the glycocalyx, and a bunch of other things that you might do along side the Zona like citrulline, which is an amino acid that, as I think, better for you than arginine. And on that note, thank you so much, Mackay, for coming in and sharing your knowledge of how you're using this, how you're seeing it work clinically, and thanks to the guys from Zona and to Mark Young, who was cast earlier, for extending a discount code to listeners.

If high blood pressure's in your family, it's in your life, you owe it to yourself to try this because this is such a low-hanging fruit of a biohack and either it's going to work or it's not going to work, and I bet it's going to work because, well, 80% of people that use it find it works. Have a beautiful day.

Mackay Rippey:

Thanks, Dave.