

[00:00:00] **Dr Mike T Nelson:** Welcome back to the Flex Diet Podcast. I'm your host, Dr. Mike T. Nelson. On this podcast, we talk about all things to increase muscle and performance, better body composition, and how to do all of it without destroying your health in the process. Today in the podcast, we have my friend, Dr. Brianna. And we are taking a huge deep dive into the world of ketones and especially the different types of ketones, supplements, both the salt and the Esther form.

If you are interested in this, you might be wondering why the heck what I use ketones. So one of the things that I believe ketones are useful. Is the end result of a longer period of fasting. When you're fasting for longer periods of time, your insulin levels go down. Obviously there's a bunch of other hormonal changes.

Also, the low levels of insulin push the body to use more fat, and if you run a PI on the fat through the liver, one of the byproducts is these keto metabolites. The three of them are bhb, beta hydroxy buterate and also acetone. These three ketones can then be used in different portions by your body.

And if you're really interested in this, I think that there is an argument for longer periods of fasting but not done all that often and done within a very specific framework. So the framework that I use for that is the framework of physiologic flexibility. So pillar number three in that is fuel systems.

So how can you further expand them out from the extreme high end, which is gonna be carbohydrate view, sitting and carbohydrate loading, maybe the use of some other supplements to help with that. And then the other extreme then is longer periods of fasting or a higher ke. To me this is the extremes of metabolic flexibility.

Can you go from a state of a lot of carbohydrates to a state of fasting or high levels of ketones? Those are gonna be the polar opposite ends of the fuel spectral system. So physiologic flexibility has four main pillars. The first one is temperature change. The second is pH changes. The third is changes in fuels.

Four is gonna be oxygen, carbon dioxide. If you get better at all of those systems, I believe that offers true longevity benefits and just being more resilient, anti-fragile, and a lot harder to kill. The result of that is your recovery is going to be much better. Also that is all discussed in the physiologic flexibility certification, which opens again on March 20th, 2023. So check it out. Go to [physiologicflexibility.com](https://www.physiologicflexibility.com) for all of the information there. And in the

podcast, as I mentioned, Dr. Brianna Stubbs and I go really deep into ketones. Ketones, esters, ketones, salts.

When should you use ketones? What are all the difference now between the ketones on the market? Shocker. If somebody says, this is a Ketone Esther, it may not be the same as a different company's ketones ester. What are some of the potential uses for them? Both for performance is where we talked about a little bit.

Then we talk about concussion tbi, traumatic brain injury, and some other potential uses. So enjoy this podcast with Dr. Brianna Stubbs talking all about the use of ketones for performance and health and possibly a role in concussion and TBI.

[00:04:07] **Dr Mike T Nelson:** How are you doing?

[00:04:08] **Dr Brianna Stubbs:** I'm doing good. Yeah. Loving life here

[00:04:11] **Dr Mike T Nelson:** in California. Where in California range are you

[00:04:14] **Dr Brianna Stubbs:** at now? I work at the Buck Institute for Research on Aging, which has been Marin and I live in the East Bay.

[00:04:21] **Dr Mike T Nelson:** Oh, okay. Nice. How's California life?

[00:04:25] **Dr Brianna Stubbs:** I would say that the weather is stellar and everything is great, but actually recently we've had a lot of storms in California, so typically the weather is great, but it's been a bit more like being at home in England.

A little bit gray, a little bit more rain the last couple of months, but yeah I can

[00:04:39] **Dr Mike T Nelson:** handle it most. You grew up that way, right? It's dreary weather all the

[00:04:43] **Dr Brianna Stubbs:** time, isn't it? Exactly. For at least six months of the year in the UK it'd be gray and raining most days

[00:04:48] **Dr Mike T Nelson:** yeah. Yeah, I spent years and years ago, I spent two months on Ireland on an exchange program.

And the running joke was, it was either rain or sun when we were there, and they're like, oh, this is beautiful weather. It's normally not quite this nice. We're like, I don't know, this isn't really that bad. So Yeah. . Yeah.

[00:05:08] **Dr Brianna Stubbs:** Yeah. But so I moved, when we first met, I was working with HVMN on their ketone ester product.

And a year or so after we, we met in 20, it would've been 2019, I moved to the Buck Institute where I still do some commercial partnership work with a company called Vence, and they commercialize keto Nesta products, but I'm also involved in the hands-on science of the buck as well.

So it's a nice hybrid

[00:05:36] **Dr Mike T Nelson:** role. Nice. And at the Buck Institute, you're looking at aging. What aspects of aging.

[00:05:41] **Dr Brianna Stubbs:** Still focused on how keto bodies might impact on the multiple pathways of aging. We are interested in ketones because fasting caloric restriction, ketogenic diet all have been shown to help multiple complexities of organism from simple things like yeast all the way up through to non-human primates.

All those similar interventions have been shown to help with healthspan and lifespan more often than not. And one of the things that's common to all of those states is the production of ketones. And so really in the last. Within the time that I've been working in the space, so like last 10 to 15 years, the prevailing like dogma has shifted from ketones just being a fuel source that's useful for the brain in times of starvation to actually ketones being a signaling metabolite that may actually also be causing some of these other, molecular effects that help with aging.

And examples of that might be affecting oxidative stress. And that was the first documented non-energy role of signal of ketones. And that actually came out of my two mentals at the Buck. Their lab that, that time they were at the Gladstone Institute, but they found that keto bodies could affect oxidative stress.

And since then people have found that ketones affect inflammation through the NLRP three and Zone, which is implicated in aging. And also post-translational

modifications of proteins that affect marker of senescence and all kinds of things like that. So it's really expanded a lot in the last 10 years.

And so my background came in with looking at keto drinks for athletic performance, and now we're interested if, keto drinks can help with healthy aging. So it's definitely an interesting pivot to go from doing clinical research on elite cyclists and all of that. A lot of the same concepts actually apply.

It's energy, stress and the body's kind of in, in the crisis as it were in extreme training, extreme environments, like I know you're very familiar with that kind of thing, what the same kind of problems apply in healthy aging.

[00:07:43] **Dr Mike T Nelson:** Yeah. So if we back up and I guess tell the listeners about some of your early research in looking at ketones and I believe it was high level cyclists, correct?

[00:07:54] **Dr Brianna Stubbs:** Yeah. So I was part of a research group that was based at the University of Oxford. The lab chief was Professor Kiran Clark and the PhD candidate met MD PhD who was running the project was Dr. Pete Cox. And they had actually been funded by the US Military as part of an op like a funding program that was called Metabolic Dominance, to demonstrate that ketones could be made in a form that would be ingestible so that you wouldn't have to be on a ketogenic diet or fasting or doing any of these kind of slow onset and, quite for some people difficult to adhere to and like kind of those kind of trying to get rid of the dietary intervention but still be able to tap into keto bodies.

And so they developed this drinkable keto source of ketones, the keto, the first keto ester. Now they're actually many such compounds. And they were testing them actually first in rowers, which is actually how I even came to be in the project because the first of exercise I love Brewer. Exactly.

So I was at that time a junior international medalist being on the under 23 British rowing team and eventually progressed through to being on the senior world championship team, winning the world championships for Great Britain and rowing. But my involvement with the ketones project was just as I was transitioning up into the other 23 national team and they were looking for elite rowers to come and take these ketones, drinks and row on their own machine with and in a blinded fashion, but with and without ketones.

And that was the first time that I ever really heard about that biology outside of a biochemistry class really got me interested. And so subsequently, did like a

master's equivalent project with the lab and we did a lot of more work on cyclists. Cause it's just there's a much bigger pool of athletes to recruit if you do cycling.

And we actually had a lot of rowers come and ride on the bike and that kind of thing. So it was just very like fit people. We did a lot of studies looking at performance, but also metabolism as well. I learned how to do muscle biopsies and all these other kind of sexy things that you do in clinical research.

But that was the first paper or I was involved in that first published paper, which came out in 2016 and the journal cell metabolism. And that was really foundational for people. A lot of people who have gone on to look at if ketones taken pre-exercise could be beneficial for athletic performance.

[00:10:10] **Dr Mike T Nelson:** Yeah. And what is. Your thoughts on that? As a side note, I did a very informal experiment with the, through the care institute, through the human performance program, where I think I had contacted you about this, where we used the old H V M N, Esther and I had students for three days. So we had 'em do, these were, relatively fit people.

They weren't elite level athletes, but we got access to a bunch of concept to ERGs rowers for non rowing people, and we had 'em do it under a fasted condition with the H V M N keto ERs. And then also had 'em do a carp load. And what we found, again, we just did this I think two or three times, it's not published unpublished data is we had a couple people hit a PR on the fasted state.

We had most people hit a PR on the carbohydrate state. We didn't have anyone hit a PR on the ketones. Although we did some very crude cognitive tasks, we did like a strop test and a few other things. And it was interesting with the ketones, we did see some trends for r p E was a little bit lower, so rating of perceived exertion cognition immediately post was a little bit better.

Performance-wise, didn't really see

[00:11:20] **Dr Brianna Stubbs:** a huge increase. Yeah, it's been such an interesting ride to watch this space evolve since that 2016 paper because at the time that was published, only the Oxford group had access to that. Yeah. Drink. And the paradigm that was set up and tested there was that the athletes were taking ketones with carbohydrate, but on the on a fasted background.

So like when I did my row machine test, I would turn up at the lab like mid-morning having not had breakfast, but then we would get your like carbon ke mixed. So it was this weird kind of, Not really what you would normally do as an athlete, but also not completely carb depleted. And so subsequently, subsequent groups that try to replicate the work, often use ketones on a background of a good carb rich meal.

And then a little bit like you just described ketones or ketones in carbohydrate. And, it's not, there's not been a consistent, beneficial effect of ketones taken before performance. So I think we're now at about 20 studies, not all of them on the mono, but a number of studies. And honestly it's pretty inconvincing not unconvincing, like inconsistent, not convincing.

Then you do, Actually, let's just stay on the science before I move to yeah. Anecdotally, like what people have done, there's still a lot of interest in whether ketones taking post exercise could be beneficial for recovery. That's an area that is pretty thread bear in terms of the research.

But in terms of pre-exercise on the background of otherwise like optimal nutrition, it seems like ketones don't consistently improve endurance performance. And not many people have looked at sprint performance, but you wouldn't expect necessarily to see that improve physically. So yeah, I mean it's, it was very striking result that we got in the Oxford study.

I, I believe that result that we got, but I actually also believe that the conditions are the pretest conditions weren't really replicating what's being done in the field. It may be that under, for specific types of exercise or now people are looking at giving ketones with, say, bicarbonate to buffer the acid load of ketones.

And there's been one of, one of the positive studies found a beneficial effects of ketones on performance there. It is possible that, we mess around with dosing, mess around with giving it a different timing or, but it's not really, I couldn't tell you a gold standard protocol that is gonna work for as many people enough of, as much of the time as they like caffeine does, right?

It's just like one of those things where it's not, it's definitely not plug and play yet. So I'm interested in it and I think that there, there may be settings where it works for people and maybe individuals who respond better, but it's not when we only have that one study. The mechanism also was very compelling.

We, we felt that, we were providing high levels of ketones for an extra oxidative substrate for exercise. And obviously providing fuel during exercise is a big possible way to improve performance. We were seeing decreases in blood lactate, which we also thought might be, improving performance and that, that kind of thing has been seen consistently in other studies.

And we also saw decreased use of muscle glycogen. And so all of that kind of together, the performance impact along with all of the, nice biochemistry and metabolism that, that we saw made sense and was quite compelling. But then again, not all of that has been replicated in the subsequent study.

So one one group in Belgium led by Peter, he's done a number of studies that followed on from the Oxford study. And on the background of regular carb beating ketones plus carbs, they didn't really see a change in muscle glycogen. So I think that, Perhaps, what we saw was because again, of like people coming in and otherwise fasted apart from that pre carb load, it's a shame that didn't replicate, reduces like the confidence in that as a mechanism.

And then the other big hypothesis was that key times were being used as a fuel and actually out of the Oxford group itself. And another, I think another group looked at this as well, but they labeled user heavy isotopes labeled isotope to label the ketones and actually measure how much of it was being burnt.

And it was under one gram. It was, oh gosh, it was really under one gram per hour. It was very like compared with carbs, which is like 60 grams per hour, it was like very small. The amount of fuel that was coming from ketones. So it wasn't even that compelling that ketones were providing like a major oxidative fuel to skeletal muscle.

And one, one of the hypotheses has always been that, you really needed to get keto levels up to provide a lot of fuel to then Be used. And this, oh study that came out Oxford was really nice actually. Cause it looked at three different dose levels of ketones and it looked at the amount that was burnt and part, and it also looked at three different exercise intensity.

David Dilo who did his PhD in the same labs, me pr authored the study. And there wasn't past a cert past like a moderate intensity and past a medium dose. There wasn't any additional ketones burnt if you exercised harder or if you gave more ketones. So it was to me it wasn't really like the final nail in the coffin, but it certainly reduced my confidence that ketones were an important fuel in ex during exercise.

When carb stores were replete. So it's been, yeah, it's been an interesting ride because early on I'd have been probably one of the strongest advocates for these as like a performance tool. And now it's not super compelling. It's one of those things about science. You have to be able to be prepared to revise your opinion based on new data.

But to then sidestep from the science, like I've been involved with companies selling these products and people come back and people buy them buy more, and people say that they do prs and that they, they, they're, I know that the companies that still make these products have customers from, the world tour cycling and I'm sure that they're measuring performance in their athletes.

So may maybe there's something going on that hasn't come out in the, n of 10 studies in a lab setting. But, I like to, I'd prefer to stick to the published data.

[00:17:17] **Dr Mike T Nelson:** Yeah. And I believe Team Sky was using them for Tour de France and for high level cyclists. And then when I. Talked to someone from that group, they said that it was more potentially to reduce the risk of head trauma.

If there was an accident, they thought having ketones on board may potentially, reduce that risk. And it wasn't necessarily for performance. And other people said, no, it is for performance. And other people said, no, it's only for certain phases of the race. And that was I never got a clear answer on that either.

And maybe it's just cuz they don't wanna tell everyone what they're doing. Or .

[00:17:52] **Dr Brianna Stubbs:** If you take, 10 steps back and look at things from a really high level, it's still quite an early stage of like technology development for this. Oh, sure. It's, so I think that all of everything that you just said could still be true if we investigated it.

There's a really good like I said, there's still potentially some performance settings where, you know, whether it's, if specific individuals or in specific, as you said, phases of the race, like maybe ketones do impact performance, less confident on that, but, possible possibility. Head injury is a really interesting area that's being looked into a lot, especially by the military.

A lot of interest in providing exogenous ketones as a quick way to potentially mitigate concussive injury. And, again, recovery as well. It's, then there's a lot more research that's needed. A lot of these things have plausible mechanisms and there's a lot of ongoing interest in work across like multiple domains,



physical function, cognitive to function, cognitive function, neuroprotection, and then, the aging and health span stuff that I'm working on now.

Yeah, it's it's too early to write anything off just yet. I think it's the best place to be with this right now is to have a healthy interest and an open mind and wait to see as the more studies are done. It's definitely no definitive answers yet.

[00:19:03] **Dr Mike T Nelson:** Yeah. If we look at just the hypothesis that it's providing a fuel source for maximal exercise and increasing performance, I believe ketones energetically are still below carbohydrates but above fat.

If we just look at the biochemistry of it. Is that correct? And would you agree with that? And then would we expect them from a pure fuel standpoint to the equivalent to carbohydrates, which probably gets into the follow up questions about signaling and other things they might be doing.

[00:19:37] **Dr Brianna Stubbs:** We can get into the weeds really quickly with that question.

There are so many different ways to rank or compare, like how things are being used as fuel. The, the one that listeners may have heard of, like ketones being, 28% or 20 something percent more efficient than carbs. That's a figure that comes from an isolated heart perfusion, rat heart perfusion.

So like a really, not physiologic and setup, but the metric that they were comparing. There is a really. Complicated concept, which is the free energy of hydrolysis, of atp metabolism. So that's like how much potential energy even gets captured and stored in the resulting atp when something is oxidized in the mitochondria.

So that, that's one thing you could compare. And let's just say based on that paper that ketones are producing more potential energy stored in a t p. But then you've got like the carbon for carbon, like free enthalpy of the molecules. And that's like another chemical way which kind of considers how much energy is stored in all the different carbon bonds in a molecule.

And then you've got the per oxygen used, how much energy is released. And so I've done this as a paper exercise before. . If you plot out these three or four different metrics, Yeah, sometimes carbs are above ketones. Sometimes ketones are above carbs, fat. Her molecule has tons and tons of energy stored in it, right?

But it's not really very efficient. But that doesn't mean, it's actually a super important fuel for most of us at rest and during like low to moderate intensity exercise. Yeah there's a lot of different ways to think about this. When ketones are present, they can't, there's not right, a ready metabolic pathway for them to be stored.

So they're always gonna be used somewhat preferentially to carbohydrate, but that doesn't mean that they're completely replacing carbohydrate. They're just being oxidized as well. Yeah it's, there's not really a clear cut answer to that. If you have carbs present, they're still gonna be boom burn at a really high rate.

But having a keto drink actually can like lower your blood glucose and like actually mess around with the availability of carbohydrates as well. It's hard to say whether that's because of the direct effects of ketones inside the mitochondria kinda being a preferred fuel versus just like changing the overall availability in the blood cause of the glucose effects.

Yeah. Sorry that was deep and

[00:21:50] **Dr Mike T Nelson:** nerdy. No, that's good because I was on panel at ISIS and years ago when some of the ketones ERs first showed up and it was right after the cell paper I think came out. And one of my concerns was if they're being marketed to general population who is not an athlete, who is not burning through, piss tons of calories at once.

What sort of happens if you consume these keto esters? We'll stay, we'll stick with those for now in a background of high carbohydrates, but paradoxically, maybe lower metabolic health than maybe higher blood glucose. Because if you look at nature, for example, those listeners know, most of the time you're gonna see high levels of ketones is a long period of fasting.

Maybe a starvation condition. Generally your insulin levels are gonna be relatively low. Yeah. Where in this case you could theorize that insulin could be high, glucose could be high, and you could have ketones also be high at the same

[00:22:49] **Dr Brianna Stubbs:** time. That's an interesting point. The, and I'll tell you the way that I think about it right now and like the data that supports that, this is just my like working hypothesis.

And so there have been studies done that last about a month, which is quite long in the grand scheme of like clinical research of ketones in people, healthy

people, but also people with pre-diabetes. And it tends to be that we've seen actually in an acute setting and in those longer studies that ketones taken in the presence of a big carbohydrate bolus actually blunts glucose response.

I think that it seems to me like at least for those 28 days that have been studied, if you're pouring in those extra carbons and calories and fuel sources, ketones, the body is able to adjust by decreasing the availability of carbs in the glucose and carbs in the blood. It also decreases the concentration of pre fatty acids in the blood as well which is gonna have impacts on tissue, insulin sensitivity, and may actually.

Potentially be, beneficial for metabolic health in the, if used in the long term. But I think that there isn't, I'm not concerned about energy overload because when we see ketones go up, TE tends to be that glucose acutely goes down even in the presence of the glucose bolus.

And there's a really neat series of studies that came out of John Little's lab in British Columbia and he took the S three through four papers and they did healthy people with an oral glucose tolerance. And ketones pre-diabetics with a oral glucose tolerance test with and without ketones. And then healthy people with and without a car rich mixed meal.

So like much more real world than the glucose tolerance test. And across all of those studies, they saw that in the keto condition that postprandial glucose was blunted. So showing again that, if you've got your glucoses here and then you put ketones in the glucose is gonna go down to compensate and keep your kind of energy balance in the blood fixed or similar.

So it's not gonna be energy overload. And then the little group as well have done these DA studies that go out to 14 days with continuous glucose monitoring and shown that effect on postprandial glucose continues for the two weeks that they have the subjects in the study. The way I look at it, the way I think that it's working at the moment is if you've got, energy level X in the blood and you pour ketones in on top, glucose is gonna go down.

Also fatty acids are gonna go down. So energy in the le level, in the blood le level in the blood is gonna stay fixed ish. So it doesn't look like we have people running around with very high glucose and very high ketones and very high free fatty acids. And just like saturating the body with substrate because it looks like the ketones themselves or have regulatory effects that maintain a homeostasis and that level of blood energy.

But, I'd, be really important to extend the work that's already been done in like a, frankly diabetic population to check that, and obviously longer studies are better as well, longer than the two weeks and 28 days that have been done. But, it's that's where the, what, where the data is right now looks like it could be.

Beneficial. The 28 day study came out, the University of Oxford, and they looked at H B one C and another marker of glucose homeostasis and a couple other things in these, were they pre-diabetic or type? They may have even been type two diabetic and things tended to be a little better metabolically in the diabetic group that took ketones.

Looks okay. Low to moderate confidence. More work needed.

[00:26:20] **Dr Mike T Nelson:** And is that because ketones are having an effect on the liver? So the liver in, in simple terms is being like, oh, we've got ketones. Oh, don't put it out in more glucose. Oh, don't put any more fats. We've got plenty of fuel here. We're fine.

Yeah. Like just cut down production of those.

[00:26:35] **Dr Brianna Stubbs:** Yeah, you hit the nail on the head. So I think that because when I've given in my like practical experience giving people ketones, the ones who seem to have the biggest drop in glucose is people who are already like, reliant on hepatic glucose output for their level.

So if someone is like overnight fasted, or someone Yeah. Is on a ketogenic diet, those people can have really huge ass drops in glucose that take their glucose into a level where they should be, like feeling hypoglycemic and they'll be feeling fine. But it's a, had its biggest impact because it's really, I think that a key.

Site of action is like delivering gluconeogenesis. And there's been some really nice work trying to tease that out. That showed that alanine, which is a key gluconeogenic substrate, alanine concentrations go down in the presence of ketones with the keto drinks. So limiting, we got alanine going down, we have lower free fatty acids, and those are hydrolyzing gluc.

Glycerol is also a key gluconeogenic Probably partially by restricting gluconeogenic substrate supply, we're getting a decrease in hepatic glucose output. And that has also been looked at with IV keto infusions and tracers showing again that the hepatic output is important, but it's probably not the whole story.

And there's probably some chain, possibly, probably also some contributions from say peripheral tissue glucose uptake in the short term anyway, because one study that was in athletes post-exercise did really depleted exercise and then gave keto drinks and infused a hyperglycemic clamps stuffing glucose into the body.

But maintaining I might get that concentration wrong, but I wanna say they maintained it like 10 millimolar very high. And the infusion rate needed on the keto condition to maintain that blood glucose was higher. And then the subsequent muscle glycogen store is also higher in the keto condition.

So possibly you're also getting some. Increased uptake in the periphery. But yeah, it's happened at either end there. You've got probably decreased liver output, probably some increased tissue uptake, and that's combining to give you the lower glucose.

[00:28:41] **Dr Mike T Nelson:** Yeah, that makes sense. I think I talked tomino and asked him the same question a couple years ago and that was his general response.

General response too. So it's, I always,

[00:28:51] **Dr Brianna Stubbs:** I'm glad I'm deviating

[00:28:52] **Dr Mike T Nelson:** too much from what Donna says. Yeah. And I'm always fascinated by one of my favorite quotes is from Peter Lemon. He is just because it's logical doesn't mean it's physiological. So we can sit around and like the argument I gave you, you could view as well.

That sounds logical. It's based on known mechanisms and nope, probably not true at all. , like you can come up with what you think. A logical thing the body would do, but that doesn't in any way, shape or form guarantee that's actually what happens. .

[00:29:19] **Dr Brianna Stubbs:** Yeah, I love that. And that really, that completely applies to everything we just talked about for the first 20 minutes about like sport performance.

Yeah. Cause it's it was so logical. Like we had this really clear hypothesis is really clear mechanism and a result that supported it. And in the end, like other studies have gotten more into, replicating and more into the details haven't born

that out. So Yeah, it's just because it's logical does not mean that it's physiological and, it highlights the importance of replication.

And, in science, this is something actually I wanna say because I feel like it should say on a podcast, I hate it when people make big claims based on one study, because you've gotta look at science as like a wall and you've gotta build bricks in that wall. And now with the experience that I've had, I think now if I came out with one study with a positive outcome, it's fine to be positive about that, but you've got a heavily caveat that really it needs replication across multiple different population groups and independent labs under different, you really, if you cherry pick data, so cherry picking is different again, which is where you might, where companies that market keto nesters now continue to say that they improve performance based on one or two of those studies, not on the totality of the evidence, the 21 studies, and that really grates with me as well.

Yeah, it's sciences is about building, building bricks over time and you can't just focus on the one like positive study that you get because that's not the totality of the

[00:30:46] **Dr Mike T Nelson:** evidence. Yeah. And the longer you've been doing stuff, you realize that man homeostasis ruins everything.

It's like you come up with all these great theories and oh, this is gonna be amazing. Sport performance, right? Look at how many, I think we've tried and tested almost what every intermediate at this point. Like listeners who've been around like, creatin probably the best one. Yeah.

Maybe beta alanine through intramuscular Carine, some buffering agents, but pipe, maybe some nitrates, all the other ones. Nitrates maybe from a blood flow. But even then Creatin has, pretty good data on it. It alanine has some good data, but not all of it replicates. You've probably gotta be in the 120 to 242nd range of exercise outside of that it gets even more sketchy.

Yeah. Baking soda bicarbonate, it can, but you also may shit your pants at the same time. Yeah. Yeah. Eh, there's always catches caffeine. But even then in the, again, best case scenario, . Yeah. You're looking at single digit percentages, right?

[00:31:51] **Dr Brianna Stubbs:** I think that having been an athlete, and you must see this having been a coach, right?

There's nothing that gets away from the basics of good training done, consistency, injury prevention, general nutrition, proper sleep. If you don't do those things, why are you spending \$40 on a keto drink? Yeah. I just, yeah.

[00:32:10] **Dr Mike T Nelson:** Yeah I feel like I, I live in this world of getting excited about new things and hoping maybe this is like the next creatine or whatever, but also having this great disc coordinates or cognitive dissidents, knowing that 99.5% of the things are just probably not gonna pan pan out either.

Yeah. But you're always kinda looking for that next thing.

[00:32:37] **Dr Brianna Stubbs:** It's, I totally agree with you. And I like, I think that we should be curious and optimistic. Yes. Cause I think it's sad if you are. Skepticism is fine, but I'm trying to think of the word. If you are, if you're down on everything Yeah.

And you are, or you know it's dead before you've even looked at it, then you know, we're never gonna make any progress. So curiosity and interest and little bit of optimism, but not over optimism. You gotta test things out, put 'em through their paces, have an open mind. That's fine.

I think that now we're talking about it, it's interesting to see interesting the nutritional interventions that you just laid out. And that in the context of, specifically with, say running the super shoes and the tech improvements in, in running have been probably like, moved the needle more than anything nutritional in the last five, 10 years.

It's just, yeah, it's really interesting to put everything in perspective of how much it's actually gonna get you. And honestly it's been refreshing to focus some of my research more on health than professional sport where, in order for those interventions have a benefit.

Everything else has to be so optimized. I think when you are thinking more about health, you accept that you're gonna be in an already not optimized condition and people are looking for things that because adherence to anything is so difficult, you get trying to get people to start an exercise regime or trying to get people to stay on a diet.

So in those instances, having as many tools as you can that are translatable could help to move the needle for people because, people's health is crummy now in, in the western world, and it's gonna cause us a lot of problems down the line if we don't fix it.

[00:34:15] **Dr Mike T Nelson:** Yeah. And last part on performance will transition is I think people forget, and myself included, just man, how long and how slow science is, especially for performance because there's some funding limitations and not every researcher is looking at performance.

It's definitely its own sub niche. Even with carbohydrates, right? I wrote an article years ago about carbohydrate loading, like the first mention of it I could find was like 1897, where they would give their athletes bread before a big event was the first sort of published thing I could find.

The, we've had a Bergstrom needle now for what, 60 plus years to do biopsies and to look directly at like how much substrate is there. And if you pulled top level coaches, I would say there's probably still not a hundred percent agreement on how much should you carb load an athlete? What should you do?

There's definitely a lot of, best practices and we know a lot more now than we used to, but. It's not like we have all of the answers and Yeah. Back to basic stuff, like even with some athletes they're like, oh, so you want me to carb load before I do a two K row? I'm like yep.

Oh, but this is so boring. I'm like, yep. And then one guy, we did an experiment where I think we took him from 200 grams of carbs to 450, just like one or two days before. Nothing crazy. Didn't even prolong it. And I think his max wattage went up by 50 or 60 watts and we did it like back and forth.

And again, he might Yeah. Be a hyper responder, who knows. But that's from carbohydrates, that's not from Yeah. Anything crazy. And he wasn't on a low carb diet. So it's, back to basic

[00:35:53] **Dr Brianna Stubbs:** stuff. Yeah. It's really interesting. And even, and this, when, now when I talk about ketones and performance and give the story and the mechanisms and where we started and where we are now I do actually highlight when carb drinks started to become a thing in the sixties with Gatorade, we're, you know what we know 50, 60 years after that now. Yeah. And we still have companies innovating on top of the carbohydrate platform. Stunt with different levels of success. Cause I, again, there's, it's really interesting. You have companies like Morten, so the company that's doing alginate carbohydrate, it, like there's a drink, you drink it in gels, it's meant to be so release.

And everyone was super excited about that for 18 months or two years. Cause they had loads of really high profile athlete ambassadors. And then now the



research is like slowly catching up. And I read a meta-analysis recently where I was like, yeah, doesn't improve performance over and above standards

And you're like yet, yet another thing bites the dust. As you were saying, you gotta watch everything with quite a bit of skepticism until it's been tested a few times, no matter how fancy the marketing is and how many high profile athletes say they're using it.

[00:37:01] **Dr Mike T Nelson:** Yeah. I think of the examples of, I don't have any disclosures on this program, so I can say whatever the hell I want, but with the SuperStarch or the waxy maze preps that are supposed to be this super Oh yeah.

Super slow. Carb release and you look at the data and you like, scratch your head and go, if it is that slow of release, how the hell is it doing anything? And then you've got, amylopectin, like Vigo that are much faster release. And even in the carbohydrate space, there's not a hundred percent agreement on the type of carbohydrate and GI upset how much fluid and blah, blah, blah, blah, blah,

[00:37:34] **Dr Brianna Stubbs:** blah.

I saw a paper recently that did 120 grams an hour, which is a, double the normal, like normal 60 grams an hour. And you're like, okay, we're gonna keep on trying. But as an athlete you just figure out what works for you and you try different things and maybe some athletes can tolerate that really high carbon intake.

So maybe some athletes really feel great on ketones and maybe some athletes really don't like caffeine. And I think one thing. That also I've feel more and more, the longer that I'm in the field is that you as an individual can try out things on yourself and if you are data driven, then you can get a sense of if it's working for you, but also especially as a female athlete, actually.

So few sports science studies done, female athletes or even in the mixed population, we have to, everyone is you can't generalize super far from studies all the time cuz you know, there's a difference between your 20 to 25 year old moderately fit college males who are, this research subjects are probably like 80% of sport studies and then even, that's being applied to women or men in their forties and fifties who are like recreationally active.

So like why are we making gold standards recommendations that are adopted by everyone based on, very constrained populations. So I think the. It's not

surprising, like you and I, we dress differently. We need to wear different clothes and so we, we also probably need different nutrition cuz you do different things to me and I'm a woman, you're, like all of those things mean that we have differences and so personalized nutrition strategies for health and performance are something that I think there's a lot of nuance missing in the conversation cuz everyone's always oh, it's a ketogenic, should I go on a ketogenic diet

And I'm like, let's let's unpack that because maybe in very few situations, yeah, like maybe it'd be the right thing for you to try, but if you are in these other situations and maybe it's not the right thing for you. Is it like good or bad? I was like, oh, the answer is, it depends. It's the same with pubs and keto messes and all of the caffeine and all of the things.

So yeah. Lots of nuance missing in the conversation.

[00:39:42] **Dr Mike T Nelson:** Yeah. My favorite, excuse me phrase, I dunno if I still it for my buddy Sean Casey, is research points the way me search gives you the answer. Yeah. No, I like that. Most people, as an individual athlete, they don't give a shit about the research. They wanna know what works for me.

And as practitioners and researchers you have to read the research cuz you gotta know what area you're dealing with and you can get more of a educated starting point. But that doesn't mean that average, which was compiled from, whatever, research in whatever people, males, females, training status, blah blah blah.

It's just a starting point to iterate from, cuz like carbohydrates per hour, I think it's what's recommended with 60 grams per hour is like the average. Yeah. And then I think it was, check Andro said that, that's trainable. You could easily give people up to 80 grams per hour. Yep. I think wasn't Kipchoge when he tried to do the breaking 200 or breaking two hour marathon, was that like 90, maybe 20 or something like that per hour.

What? Maybe he trained his way up. Maybe he's just, the guy's obviously an outlying freak anyway and he is trained very hard. Maybe that's just something else that makes him run faster too. I don't know. Yeah. But you've got almost a two full difference between the average and like the elite of the elite in Yeah.

Dr. Carbohydrates, again, something that's rather basic, . Yeah,

[00:40:59] **Dr Brianna Stubbs:** exactly. Yeah. Always more to learn. So I make a far fewer definitive absolute statements than I might have done at the start of my career. Yeah.

[00:41:09] **Dr Mike T Nelson:** Yeah. As we transition more into, to health, can you just run down the codes?

There's a lot of exogenous ketones on the market, some are not on the market anymore. Like how would you classify, the types and if you would generalize them between the Esthers and then also we've got the salt variations of them as Sure. Supplemental

[00:41:30] **Dr Brianna Stubbs:** form. Yeah. Like the, like most basic way you can supplement ketones is Having fat based products, so like medium chain triglycerides that will like slightly elevate your ketones.

Those tend to be the least efficacious in terms of blood keto levels and have a relatively high gi side effects risk. That's the kind of thing that people are putting in, like following a ketogenic diet, doing bulletproof coffee with fat and medium triglycerides. So that's like most basic, least efficacious probably most broadly available when you can get that kind of supplement most places.

Then we have keto salt. So they were one of the very first things to be commercialized and it's you just have the main keto body that's in the blood beat, hydroxybutyrate in an ionic form with a mineral like sodium, potassium, calcium. Those products are evolving. So the very first load that came out were what's called Acemic mix of the two optical isoforms of beta hydroxybutyrate.

You think of this like left-handed and right-handed forms, so like structurally the same but don't overlay in one another. Yeah. And only the right-handed form is used in the body. We don't know much about what the left-handed form does. Again, initially, back when I started researching this field, we thought that it didn't do anything.

And now people are finding that this left-handed form may actually have some of the signaling effects. So we, like maybe it's doing more than we think it is, but quite not unknown about that. And so when we were giving people salts and measuring their blood ketones we're only measuring the right-handed form.

And so keto levels are pretty low in comparison with other products that we'd studied. And people haven't consistently seen performance benefits with that kind of product. So it's better than medium change triglycerides, but still not

super efficacious. And there's been, I don't know how much of this is like accurate, but some people express concern about the possibility of impact of long-term and mineral consumption.

So if you're, really like tripling your daily sodium consumption, if you don't, if you're not changing your diet to take it out from somewhere else, you run a risk of mineral overload. Could affect your blood pressure, could affect kidney health otherwise. So that's never, these products have been distributed for years and as far as I know, when no one's dead.

So it's maybe more of just like a concern, a worry than a real thing. But that's, a consideration. And I also found that when we studied those. When you were using like higher doses of salts, they could also cause GI issues. A little bit like bi carb, right? If you'd load a load of mineral into the gut, you just, your gut's and yeah.

So I had to have, it

[00:44:08] **Dr Mike T Nelson:** feels horrible too. It just doesn't feel good. .

[00:44:11] **Dr Brianna Stubbs:** I actually had my sister come and be a research subject for this study where I was studying the high dose of salt, and she never came back and did any of my studies again after she took the high dose of salt. She was yeah really glued to the toilet for a few hours.

Yeah that's why don't you family members in research so that's a salt bucket now. Companies have started to develop forms that are just the right-handed form. So the measurable amount in the blood is actually higher. With those products, you still don't get around the mineral problem.

It's but that's like an evolution on the first round of products. Not all products are purely this right-handed form, and sometimes more often than not, the companies obscure like actually what's in the products. Not super sure whether it's the physiologic form or a mixture of the two.

So though there's a big category of products based on keto salts, and then there's a bucket of keto Esthers. And it used to be that there was only really one or two that were talked about. And now we're at least three, actually four, not so at end, they don't all behave the same. So I think. At the very start describing this category.

I have to say, just because something is a keto ester doesn't mean that it's all, they're all gonna behave the same. These keto esters tend to be made up of ketones or keto precursors that are as terrified to one another. A common like backbone for these molecules as an alcohol called one three butane dial.

And that's actually itself. That one three butane dial is now also being commercialized by a number of companies as a way to elevate ketones. We can talk more about that in a minute as well. But keto Esters get around the mineral problem. They deliver the ketones and keto precursors into the blood in a sort of a more, it seems to be more consistently potent way.

So across the different Keto ES supplements, they tend to generate higher levels of ketones in the blood than the salts. I'm just gonna get rid of these.

Can you hear me again? Yeah, we can hear you. You still coming?

[00:46:21] **Dr Mike T Nelson:** Nope. Can't hear you now. Oh, now you can there. No, we can.

[00:46:25] **Dr Brianna Stubbs:** So let's talk about, let's talk about three examples. One is the Oxford Keto Ester, the, it's called a BHB mono ester. This is the one that we've just spent most of the first half of podcast discussing in terms of sport. It is so a mono as one Ester bond and it's B hydroxybutyrate.

That main keto body that circulates in the blood is terrified to that alcohol that I just mentioned, one three butane dial. And so it's a really simple molecule. It gets cleaved in half and the B H B hydroxybutyrate is released directly into the blood and the dial undergoes a couple of conversion steps, like via normal alcohol metabolism pathways in the liver, and then that ends up as beta hydroxybutyrate as well.

This is the most widely studied keto ester's been used in sport performance studies, glucose metabolism studies studies of diabetes and some neurocognitive studies as well with, quite a lot of interesting results across a lot of these different benefit areas. So that's I guess the gold standard with keto esters and science as it stands right now that's commercially available on being sold by a company called T Delta s.

And keto also commercializes that as well. Next up we have a di ester, so two esters acetate and butane dial. So it has two parts of CTO acetate, both are tied to a central butane dial molecule. One thing I should say is the esters are

really like generic. We consume a lot of foods with esters, so it's nothing really special for the body to break up these molecules.

The aceto acetate dista was developed by Domino's Group at U usf. As far as I know, it's periodically being commercially available, but not really very widely distributed. I know a company called Keto Logic was making it and selling it in soft gel caps.

[00:48:06] **Dr Mike T Nelson:** Yeah. That kind of disappeared, didn't it?

Yeah,

[00:48:09] **Dr Brianna Stubbs:** it was on Amazon and then not on Amazon. It's doesn't seem to have a stable supply chain. I know that, and I don't whether they still are, but they were running clinical studies Inman's disease, so they're interested to see whether some data comes out of that or whether they make further efforts to commercialize it.

But I'm going to be running a study using some of that as to shortly, so hopefully data on it. So that molecule is gonna deliver, not bhb, but a lot of aceto acetate. That's the second most common keto body that is in the blood when we make our own ketones and bhb and aceto acetate uhum with one another.

So when you deliver the aceto acetate, some of it's gonna end up as bhb, but they're gonna interchange between the two. Without wanting to go too far, like down, like too much of a rabbit hole. The conversion is redox linked and so as to drive one way or another, you're gonna be having different physiologic effects on the body.

So delivering a ton of bhb like with the mono, which it only delivers p versus delivering a ton of aceto acetate with that dier. Could potentially have quite different effects on the body via both redox, but also one of the leading researchers in ketones and signaling is called Peter Crawford, and he's done a study showing that aceto acetate and not be hydroxybutyrate differentiate affects macrophage, so immune cell function.

I su suspect that in the, in the next 10 15, sometime we will end up dosing with or choosing different keto esters or different keto nutritional strategies according to a specific target pro product profiles specific desired endpoint, where in some cases C2 Aate might be more beneficial.

And actually, interestingly another example of this is I can't remember whether he published this data. But you should talk to Don Stein around this. He used the CTO Aate Esther in his seizure model, and it was very profound suppressing oxygen induced seizures. And the BHB mono asta did not.

And he suspects. That's because of Redox. And again, you know how those different ketones are being metabolized. So not all species of ketones are equal. And then

[00:50:17] **Dr Mike T Nelson:** I think that's why he went down, if I remember correctly, from talking to him down that route, looking more at that Esther type because they were looking at oxygen toxicity and some of the other stuff too.

So I think that's why they patented and went more down that route.

[00:50:32] **Dr Brianna Stubbs:** Makes sense. And I think that, it, it makes a lot of sense to me that delivering BHB is gonna be different to delivering aceto acetate. Yeah. Be useful. One could be more useful for say, physical performance. One may be more useful for neuroprotection.

And we know that the ketogenic diet helps control seizures. And people suspect that's actually more due to these CTO acetate and acetone, those keto species than it is with vit hydroxybutyrate. It's still like at the hypothesis kind of stage. I wouldn't be surprised if we end up with different keto strategies for different therapeutic outcomes.

So those are two examples. One mainly delivering bhb. One mainly delivering aceto acetate. And then there's one that's in the middle, which I've been working on for the last couple of years, which is butane dial again, dier of fatty acids. So a bit like the mc t oil except supercharged induced and much more effective at increasing blood ketones than a matched amount of mct.

But, and in this case, cause you're not delivering the ketones directly because you're delivering the fatty acid precursors to ketones, you're actually triggering ketogenesis or leading to ketogenesis in the liver. And that's very distinct to those other two keto nesters cuz those two just directly deliver ketones into the blood.

But in this fatty acid with this fatty acid ster, it gets hydrolyzed, you dump a load of fatty acid onto the liver medium chain. So it arrives quite quickly. And then it then is a substrate B oxidation produces a load of a settle co a that a settle

co A is used for, oxidation, but also for ketogenesis when it's being poured in at a high enough rate.

And so with that we see this is interesting. So we'd only ever really measured B H B with this compound, but I'm very interested to measure acetyl acetate.

[00:52:18] **Dr Mike T Nelson:** It should be higher, right?

[00:52:18] **Dr Brianna Stubbs:** It should be higher than the mono. It should be intermediate between those, right? So it should be more like the physiologic ketosis that you get when you produce them yourself.

Cause you're producing them in a physiologic ratio. And so I guess to culminate like the section, actually you should just briefly talk about butane dial. So now companies that have taken all of the other precursors off and are just commercializing the butane dial, and so there's no like traditional keto precursors like fats and no ketones, no bhb or C two acetate.

You just deliver this alcohol. And it does raise B h B, but it's not known how, it's a lot few, many, a lot fewer studies on that. We don't really know even the kinetics of it in terms of. Blood ketones. So it's it's a bit of an unknown quantity right now. But that's so the C6 Astor is being commercialized by a company that's in partnership with the buck called Vence.

Butane dial is being commercialized by H VM N and by Keto Aid as well. So those are like the main companies playing in the space. So my big research question and it's part of a collaboration that's funded by the military and getting to be run in collaboration. Actually Buck is collaborating with Ohio State at the prime awardee on this military contract.

And so what we are gonna do is take all of these different compounds that we just discussed, actually not the salts, but the BHB mono are middle of the grounds C six, fatty acid keto esta are various CTO, aate based Esther from DOM'S Group, and then also butane dial. And we're gonna study those all side by side.

We're gonna measure everything. So we're gonna measure not just the b h b, we're gonna be using very cutting edge mass spec and taking very careful care of our sample to actually get at C2 Aate as well. And the C2 acetate is really unstable, very difficult to measure, and that's why it's not reported in almost every study of keto science.



It's really the ugly sister forgotten, but it's a huge part of the picture. That's just missed because it's technically difficult. So BHB CTO acetate, one other thing that we think could vary is pH. So we know that pH responses. We know that the BHB mono results in metabolic acidosis.

And that's actually thought to be some of the reason why it does some of the things that it does in some of the hypoxia experiments where it's been studied. So it's interesting we'll see if that whether there are whether there's a generic generic set of. Physiologic changes that occur with all ketones or whether some ketones esters, or some ketones.

Supplements do different things and ultimately because at the moment, all the companies that make these, they all just talk about raising ketones. And that's about as far as it gets. But for the military and for athlete practitioners, and for those of us thinking about, health or neurocognitive health or any specific outcome, we actually need to know whether there's a differential kind of fingerprints of each of these compounds.

So we're gonna do it, do the study at two dose levels, which I think is really important as well to see if there's a dose response and compare across yeah, all of the keto measures. A bunch of strong iron, acid based balance some respiratory gas analysis as well. It's just a very detailed, resting characterization of the physiologic effect of these different compounds.

Hopefully once that works complete, I'll be able to tell you a bit more about whether these are all like, yeah, all ketones es it's just the same, you take one ketones and it's the same with all of them, or whether I could give you more specific recommendations about which to use endpoint.

[00:55:47] **Dr Mike T Nelson:** Oh, that's awesome.

I'm super excited to see what the end results of a study is because it's, looking at the research is an outsider. It's hard because there isn't a lot of direct comparisons. Yeah. It's like this lab did this and we found this and this lab did this and this subjects, and we did this in the rat model and we did this in the mice and we did this in humans.

And so you're like

[00:56:06] **Dr Brianna Stubbs:** loads of especially the animal papers gloss over what compound they use. There is

[00:56:11] **Dr Mike T Nelson:** a number of Yeah. That was fascinating to me. Yeah. It's Hey what did you do? It's ,

[00:56:14] **Dr Brianna Stubbs:** they use assault? Did they use, yeah. And then it's used to make generalized statements about like ketones as a whole.

It's really interesting actually with butane dial because there was one research group that used butane dial, and if you read their papers in time order, they start off by talking about it as oh, we use butan dial to raise keto levels. And as you go through the papers, they actually started doing butane dial and a different ketones separately.

And they were finding that butane dial did some things that the other ketones did not. And they actually then ended up testing butane dials effects on vaso relaxation and vaso constriction. And they found that butane dials specifically not B h b, was having some of these effects on the blood vessels.

And they'd been using butane dial all the way through and making quite general conclusions about like keto effects, when actually it was, it itself was having effects that they hadn't really accounted for. Yeah it's. You've probably seen this if you follow the diet and nutrition space, especially in like animal studies.

It's like high fat diet does this to rodents. Yeah. And so then people are like, oh, that means that the ketogenic diet in humans ugh, bad. And actually it's a high fat diet for rodents still has, it's te more typical Western diet still has quite a lot of carbohydrate and it's get a rodent in ketosis.

They have to ba basically no carbohydrate. And if you haven't verified that they're in ketosis, then you can't really extrapolate like a high fat diet conclusion to a ketogenic diet. And, you see this all the time. It's the same with keto.

[00:57:39] **Dr Mike T Nelson:** Yeah. I, at this point I was just did this yesterday.

I was looking and whenever I see something that says high fat diet and rode. I don't even read 'em anymore to be honest. I just, and just skip right over it. Cause I'm just like, this is gonna be a trash bin fire most of the time. .

[00:57:56] **Dr Brianna Stubbs:** I agree. And even just I got so burned, like watching there was a researcher called Emily Goldberg and she was doing some research on the ketogenic diet and someone went in and really tore her to pieces for not protein matching.

And there's so many like nuances. It's oh, if you haven't held protein constant, then does that affect the ability to make this or that conclusion? And you're like, yeah, there's a lot of like nuances in designing diets for rodent studies.

[00:58:23] **Dr Mike T Nelson:** Yeah. And her good friend Tommy Wood loves reading animal research.

He's such a huge fan of it. I'm totally kidding. Yeah, he's on another podcast for, and he does animal research on ferrets and other animals. And he's oh,

[00:58:37] **Dr Brianna Stubbs:** I know, of course I know Tommy, me, he and I actually work through paper together. He's doing the statistics

[00:58:41] **Dr Mike T Nelson:** for me cause I'm not working. Yeah.

No, he's awesome. But he's eh, like 80, 90% of animal research, that's how it's done, is just trash. And he actually does animal research. So

[00:58:50] **Dr Brianna Stubbs:** cross house and he can go away. Go ahead on throwing those

[00:58:52] **Dr Mike T Nelson:** stones, yeah. So he is the, i he can say that I get in trouble if I say that . Oh, I just threw him under the bus.

The one three butane dial, like I got an early sample of that years ago from a guy in the supplement industry who will remain nameless. It was freaky because I had talked to him. And he's Hey, you wanna try and do a supplement? I'm idiot me. I'm like, sure. And he is I'm like, what is it?

He's I can't tell you. I tell you, it's grass certified. So generally regarded as safe, it's non-hormonal. Gimme your address. I'm like, okay. And I had talked to this guy off and on for five years, never met him in person. And I get this little vial of a liquid in the mail and he puts in this good grips, like measuring glue, measuring thing that he picked up at a Home Depot in there.

And that's it. No return address, no c o a, like no nothing. Yeah. And I'm standing over my kitchen sink and all I remember him telling me was, he's and for God's sake when you take it, don't throw it up because it's really expensive. And so I like left it and debated for a while and eventually tried it and it, oh God, it no smell.

But it did not taste good at all. It was just horrific. Yeah. And later I find out that's, Actually what it was. But all that to say, like my buddy Ryan Baxter has done a couple measurements recently looking at BHB levels with it. Do you think it will raise b h B as high as some of the other Esthers or, cause it has to be converted and what you're starting with as a base material?

Yeah. Maybe it's more variable from one person to the next or Yeah, who knows?

[01:00:27] **Dr Brianna Stubbs:** Yeah, there's a lot of unknown. Something that's g graded with me a little bit is that it's being marketed as an improvement on the asta technology. When actually Yeah, like it is, like it's not, it's, I thought it was a step backwards almost.

Yeah. It's like we've gone from V1 back to zero, no, 0.5. Like it's cheaper because you don't have to do like the certification process. Yeah. It's way cheaper. People are saying it tastes better. I don't agree. I think it still tastes No, they all

[01:00:50] **Dr Mike T Nelson:** taste

[01:00:52] **Dr Brianna Stubbs:** horrible. It still tastes bad enough that I don't wanna have it in my mouth.

No.

[01:00:55] **Dr Mike T Nelson:** No.

[01:00:57] **Dr Brianna Stubbs:** don't, like it doesn't taste that much better. It is cheaper. It, I've piloted it myself. It can raise keto levels. It seems to be like a little shorter acting than the esters. You probably because of the taste and the. Whether or not it makes you feel drunk is something that I've had debated.

So I've heard some people, and I've taken a couple of bigger doses of it myself and been like, a bit like, woo, like that's reported in there's only two published papers right now. Both of them report people feeling like intoxication like symptoms. But I really don't wanna get too far out, like over the tips of my skis because, maybe it should just be used at lower doses.

The forms that are being commercialized now or the pure r butane dial, maybe different to the Rs. So and maybe again, this is like individual variation and I think this is really important to say, and I know that the company's selling the

butane as. It itself is half of the mono ester, a third of the C6 fatty acid, Ester a third of the aceto acid, Ester.

So it is in all of these other esters. So if it is, it can't be, it can't be that bad cuz it's, if you take 25 grams of the bhb mono ester, you're taking, 12.5 grams of butane dial once. This is terrified. So it's unclear. It's unclear, I don't know. I think that it, I think it's probably a little over simp.

Simpler, simplistic to just be like, it's gonna behave the same, a 25, if you think that you've got 25 grams of butane dial, 25 grams of bhb mono ester, I think that the increased flux through the alcohol metabolism, past the pathway, we've measured it with the fatty acid ester and in animals with the BHB mono ester, you do get.

Plasma circulating levels of the butane, the alcohol itself, butane dial and other people other researchers in the nineties found that butane dial is very like permeable into the CNS and does cause CNS effects. Maybe doubling the amount is gonna increase the amount that you see in the blood.

And maybe that is gonna be having some effects. As I mentioned, there are some specific beneficial, maybe effects of butane dial on, the vasculature. It's this stage there's a lot of very definitive statements being made with people with like skin in the game. I know that there's some kinetic data pending on the butane dial.

I'll be really interested to see that. And I know that there's some performance data pending on the butane dial, so I'll be interested to see that. But this stage, when we go back, if we go back to my, like bricks in a wall analogy, that's still only gonna be like four published papers on this compound.

There's every reason to suspect that it's not just the same as taking the HB cause of the alcohol metabolism component, whether that's cause of a liver effect, or whether that's because of release of butane dial into the circulation and then effects of the butane dial systemically or in centrally in the brain.

I, that would be my that's where I sit right now. I'm perfectly ready to like DECAMP and move to a different position. like changes, but it's just I don't know, I dunno how I'd feel about taking like 50 grams of butane dial a day versus something else.

[01:04:11] **Dr Mike T Nelson:** Yeah. Cause I find it interesting that you've got one company marketing it as towards iq, cognitive, and then you've got another company marketing as a alternative to alcohol.

And I'm like, true, right? So I'm like, wait a minute. Cuz I looked at this again the other day and I'm scratching my head going, is this a different, isomer is a different dose. It appears to be very similar. I think. Yeah,

[01:04:36] **Dr Brianna Stubbs:** it's the same. Definitely some truth has gotta come out there. Not from the companies, but from people like using it in research.

I think so, yeah. Couldn't say hard to say. I think that the most important thing that we need first of all is the b h B effect data. Cuz at the moment it can't, we can't even say for sure like how it works on key keto levels compared with other. And then, we need more like tolerance data.

At the end of the day it is, as you said, it is grass. It is generally recognized as safe, so I'm not con super concerned about safety

[01:05:10] **Dr Mike T Nelson:** there, it seems. Yeah I'm not super worried about safety, just more, it seems like it's being marketed for like completely different effects, which Yeah.

Boggles the mind, .

[01:05:19] **Dr Brianna Stubbs:** Yeah. At the end of the day, everyone just, all those guys just wanna sell it and make money. They the thing that I see that generally annoys me about the whole space, including the salt space, is a lot of people co-opt and cherry pick the one or two positive studies that are not even done with their supplement and they co-opt those into product positioning.

It's something when I work with companies since since moving on from my first role, the way that, we now look at evidence is much more of a, like a totality based. And, you don't make definitive statements about the product unless you can look at all of the literature and have a, file that backs that up.

So just different ways of the thing is, as supplement industry, not super well regulated food industry, not super well regulated. And so people are gonna say things until they get told off. But this is a really interesting, the beauty dial is a really interesting case because of the way that it tiptoes around the do you need to be 21 to buy it?

Yeah. Cause you know I wonder if it, I wonder if it'd ever be a big enough fish to get the attention of someone Reg who's a regulator. Cause it's definitely interesting cause it walks that line if you're gonna as a

[01:06:26] **Dr Mike T Nelson:** buzz. Yeah. And the we'll just say the guy who sells the hard ketones is quite a interesting fellow.

I will leave it at that. Yeah. and the whole supplement space is filled with, Interesting fellows and probably that was not gonna change anytime soon, .

[01:06:48] **Dr Brianna Stubbs:** That's why, for me, I enjoyed, I think I was in, in industry, pure industry for three years and it was, I learned a ton and I think that it's important for scientists to know, like how to translate ideas cuz you know, scientists get stuck up in an ivory tower and you don't know how to, like what goes on in the real world that, that brings science to the masses.

And so it was really helpful and really enjoyable and I learned a lot. But it just great when you can't answer the questions yourself because of some it kind of conflicts with a business interest or there isn't, or just isn't budget for it. It's nice to now be in a role where I can advise companies and provide scientific support but also, Just ask like interesting science questions as part of my day-today, job as

[01:07:34] **Dr Mike T Nelson:** well.

Yeah. And remind me what was the very first ketones Esther h v m N had, was that a mono Esther also?

[01:07:42] **Dr Brianna Stubbs:** Yeah. Yeah. Oxford University NIH developed the mono ster and Right. The company, the like how B IP at Oxford was called T del Pers . And so they initially licensed it to HBM n and I moved from doing I PhD at Oxford under the CEO of Ts, who is the professor.

I moved and helped H VM n launch it. And so that first product, h vm n Keto, which looks like this, yeah. Was mono asta, and then I left Hvm. The license agreement between a TLS and H B N finished and tls ah, launched their own version, which looks like this. And so this is tls, this is the original company that the Oxford professor was running, and she went and launched it herself.

And h om n lost the rights to make it. And so for a period of time, they didn't have an offer offering. And then I think actually this one that I have they called

it Keto 2.0 to start with. I have all the bottles of everything, yeah. Yeah. actually for I should wave the luminescence one around just so that I've shown.

Yeah. And actually, oh, do I have, I think I have some keto aid as well here just to be Oh, yeah. But yeah, so then HBM called it 2.0 and now they call it Keto And that's just like the butane dial, which as we said is not really a 2.0 or more of a no. Point five in terms of in terms of technology, I guess they would say, like it being cheaper and it tasting better does effectively make it an improvement, but yeah.

Yeah. Not I'm not here to argue with that

[01:09:06] **Dr Mike T Nelson:** yeah. Yeah. I didn't realize they had removed it. Cause I got a call from we'll say a couple months ago from a good buddy of mine who's a neurologist from a certain N F L player who got a concussion. And so they're asking me all these questions and stuff and I was like, oh, here's, your options.

And I went to their website and I'm like, oh, it's not, yeah. There anymore. And it's

[01:09:28] **Dr Brianna Stubbs:** really, yeah, I don't wanna get into this too much, but it's like it co-ops a lot of the brand building and studies that were done on the Esther, including when I was there, we secured investment from the military to study the Esther.

All of that money was given to study the Esther and that credibility is being leveraged to sell the Butte dial as an improvement, which I don't

[01:09:53] **Dr Mike T Nelson:** really agree with. Yeah, I will tend to agree with that. Related to concussion so I've asked this to Tommy, I've asked this to Dom and other people.

I have this crazy thing where if I'm doing kite boarding, then I get dropped outta the sky, 20 feet in the air. Generally, we're a helmet, there's a risk of, that or a car accident or hopefully I stay away from trees snowboarding. But one of the things I do is I carry a keto Esther with me, my thought mean I would consume the ER after this.

Again, just me talking, this is not medical advice. After I, potentially maybe have a concussion on the way to my neurologist who's a good buddy of mine,



who I actually have on speed dial, which is nice. I would consume the keto ester, put myself in a state of ketosis, and I would transition to a ketogenic diet.

Yeah. Based on the research. Do you think that's a good idea, bad idea? Who knows? Might be helpful. Dumb idea. .

[01:10:49] **Dr Brianna Stubbs:** The truth is who knows, but basically based on the preclinical evidence, I'd say it's a good, or I'd say it's a best good and it at worse nu net neutral thing to do. There's a quite a lot of compelling evidence in animals with different concussion models that being in ketosis, either at the time of the impact or post impact as well, can reduce infarct size, reduce brain swelling, rescue brain at p.

Now, you know this as well as I. Very hard measure. Concussion in humans. Yeah. Can't administer them in a research setting. Yeah.

[01:11:30] **Dr Mike T Nelson:** That come into my lab, you get a concussion, you don't, and we're gonna see what happens. Yeah. So

[01:11:36] **Dr Brianna Stubbs:** it happens in the real world. They all happen with different impact, different parts of the head.

There's different like timelines, it's just it's a really hard problem to get at. Very important problem because it happens in the playground all the way through to the workplace. All the way through to, yeah. So like it's a huge problem that I have a really big interest in.

But I, I'm not an expert. I have no idea how to tackle it. But I think that the hypothe, the mechanism, For both energy provision, reduction of oxidative stress and inflammation, and actually increasing blood flow in the brain as well. Like all the things that we know that ketones do in a preclinical setting, and many of which we see transferring into a clinical setting.

We know from studies in people with cognitive impairment that the brain avidly uses ketones, even in the ab the presence of suppressed glucose metabolism. So even a brain that isn't able to use glucose can still use ketones. We've seen that keto, that the keto nester can increase blood keto levels and affect like the way that the brain is functioning when you look at it with an FMI scanner.

And that's, so I think that if something like that happened to me or a family member of mine, I would also tell them to do that. But it, How we get to having like clinical evidence. It's a like a hard path to map, but I don't think, I can't see

a downside unless, unless you wanted to argue that glucose is a really important substrate for the brain.

And so if you're limiting glucose, then that's, potentially worrisome. If so long as you're providing ketones, as this, as the alternative, I think that, it should be a good strategy. And I know that there's a I think that I was involved in a funding application that wanted to look at this in a clinical SEC in a clinical setting and I'm not sure whether that is going ahead or not, but hopefully it is because that's really important work.

[01:13:30] **Dr Mike T Nelson:** Yeah, that was, that's kinda my thought is we have a pretty good idea of what the potential downsides are. I don't think there's a safety issue as far as I'm aware or anything like that. Do we know what the real potential upside is? It's unknown, but we've got. Some early data, some preclinical data, some mechanistic stuff that says, eh, seems like a good idea.

But

[01:13:52] **Dr Brianna Stubbs:** one thing that I'm surprised it's taken me this long to say on this podcast is that a huge unanswered question across performance choice of ketones, supplements, and also in a clinical application like TBI, is like, what level of blood ketones do you need to

[01:14:09] **Dr Mike T Nelson:** be at? Yep. That was my next question.

[01:14:12] **Dr Brianna Stubbs:** Yeah. That's like holy grail for this field. Defining that. Probably different for different outcomes probably. So yeah, I. To go back to our like choice of supplement question. If the threshold for TBI is actually only 0.5, then it doesn't matter if you use a salt or a, or whatever.

Like it doesn't really matter, just use anything. But if it's actually, two millimoles, then yeah, you need to take something that's gonna get you higher and dose it in a way that's gonna keep you there for some time. Unless, cuz you know the second question after dose level or B h B concentration.

The second question is amount of time. Is it something where you just have to kiss it for 30 minutes and then you hit, some signaling pathway and you get a benefit? Or do we actually have to sustain keto levels above a certain threshold for time? So these are really big and important questions and I'm a little concerned.

That studies may have null results because we haven't got that dialed in because actually we've also been assuming generally that higher is better. And that's the, marketing position that the mono er took to start with. It's like we are superior to salts because we deliver a higher B hydroxybutyrate with the mono than is possible with MCTs or salts or with anything else.

But, to go back to the paper I told you about that showed that past a certain dose, more of it wasn't even being oxidized. So it really blew that idea that higher is better out of the water. So you know, now the more like, trendy way to talk about it is that there's like a goldilock.

So in the middle that's neither too high or too low. But that's again just like speculation. Not super. We need good like dose response studies. We need to find an n a pd, a pharmacodynamic endpoint that reliably changes and then look at it across like multiple doses and see whether, we know that for some things we have started to do that.

With heart function, there's been infusion studies that have done step rate infusions and showed that the higher that the HB gets, the more that cardiac output changes. So that's one example where it's okay, yes, higher is better in the short term for cardiac output. Maybe we need to do the same for brain blood flow or some of the brain functional connectivity measures that have been done with one isolated dose level.

Lot of speculation about that as well.

[01:16:39] **Dr Mike T Nelson:** Yeah. And so right now I just have the old H V M N, the first Esther, but I'm. Running lower, so I'll probably need to replace it again coming up .

[01:16:48] **Dr Brianna Stubbs:** Yeah, you should try like the C6 fatty acid dester. It's maybe I don't know, a different kind of bad taste.

[01:16:53] **Dr Mike T Nelson:** It can't be any worse than that original one. The original one with no flavoring. That was a horrendous, and I know that I have people take it that, that we used to take videos of their face. They're like, they look like they all got poisoned .

[01:17:06] **Dr Brianna Stubbs:** And I know that within, I know that the, our partners at Ju Essence are doing an awful lot of work on taste and flavor.

So like hopefully they'll be some of more stuff like can share about that sometime in the next like few months. Cuz that's, at the end of the day everyone that's playing in this space, whether they're like, whether they're right or not believes that this is like quite a powerful metabolic intervention.

Nobody quite knows like how to get there. What we are seeing consistently with almost all these supplements is that like you can give them and within 30 minutes you're in this quite. Unusual state of fed ketosis and cause of like spotty clinical literature and a lot of preclinical literature we're like this is interesting.

We're all just like trying to figure out what it's good for and make products that like actually are useful in the field. Because I argue that, whilst you've got something that costs \$30 per serving and tastes like gasoline, it's neat, but it's not it's just not translatable and really with the butane dial, I'd argue that's still not fully fixed.

It's ch it's cheaper, but it's still done. Tastes good. And so what we need is something that is comparable to like another other supplements in terms of like cost per serving efficacious in terms of delivering our like unknown vhb threshold, but doing some, doing something in the blood and tastes good enough that anyone that I could go and give it to someone on the street without the prime.

Cause like right now, every time I give someone a keto and I'm like, okay, this to drink, but it's gonna be like top five worst things you've ever tasted in your life. And you, and if you tell people that normally they'll drink it and they'll be like, oh, that's bad. That's really bad, but thanks for warning me.

But if I gave someone like the Veces product, they call it chocolate Nitro. And you look at it and you're like chocolate milkshake, , it's good. And if you don't tell people what to expect, people's people are just like, are you trying to poison me? So you need something, like somebody in the space needs to get to a point where you can hand over a bottle, watch someone drink it, and they don't change their face.

So until we do that, all of this interesting science just isn't relevant. So that's why clients needs good industry partners because we can, e even if I found out tomorrow that ketones were great for concussion, it would still be a really hard sell if it tastes like it did and was expensive.

[01:19:23] **Dr Mike T Nelson:** Yeah. And it's one of those things when you taste it, you, I hate to use the word chemically, but it has a very chemically,

extremely astringent, like almost like this. I think I might have poisoned myself. It, it doesn't have anything you can relate it to other than something that's really bad.

[01:19:42] **Dr Brianna Stubbs:** It's certainly cause people will compare it to things that I'm sure that they've been ever actually tasted. They're like, it tastes like nail polish remover. And I'm like, you've been, yeah.

[01:19:48] **Dr Mike T Nelson:** You've drunk nail polished remover , or

[01:19:50] **Dr Brianna Stubbs:** it tastes like paint stripper or some other things that like you just Yeah, you never drunk that categorically otherwise you wouldn't be here, but yeah it's or gasoline.

Yeah they don't taste good right now. And that's a big barrier to implementation.

[01:20:03] **Dr Mike T Nelson:** Yeah, interested in full disclosure, I do have a program through the KE Institute that talks about the use of ketogenic diets and supplements for T B I and yeah, and the data. And the main reason I did it is was hoping different neurology, clinical neurologists would least publish some case reports as a start to be like, hey, cuz one of the issues, with doing therapy right away is your brain just has inflammation.

It's got a low energy. Like you can't even sometimes do a lot of work per se with it. So hopefully this would be an alternative that, that might be helpful for them to start doing therapy sooner too. Yeah.

[01:20:39] **Dr Brianna Stubbs:** I'm, Would love to discuss that with them and anyone on your program that that's doing that kind of thing.

And, we at the Buck Institute we're using a mouse model, but we're looking at ketones and delirium, which is acute confusional state in older people. And it's a huge problem in clinically. And I think that, and actually a lot of similarities where it's like acute brain metabolic crisis and inflammation.

Not through a physical injury, but just, from the lack of resilience capacity that, that they have. It's an area that's being attacked from multiple angles, whether it's TBI or delirium. And hopefully someone will, get something that translates to the clinic soon.

Cause I think it's, it just makes so much mechanistic sense that I really I'm still working on this field and I hope I continue to work on this field for a number of

years. I really think there's gonna be like a blockbuster or maybe even two blockbuster, like use cases for ketones.

These really powerful interventions, like it's gonna, it's gonna work really well for something. And I'm just really excited to see what that is.

[01:21:36] **Dr Mike T Nelson:** Yeah. If I were a betting person, I would bet on T b I if I were to bet. And again, that's it's a guess at this point, but if there was anything related that's probably where I would put my money.

Yeah,

[01:21:50] **Dr Brianna Stubbs:** I'm with you. I'm with you. That would be in, in my top, like in my top three. And one of my other top three would be heart failure. Cause it's, so there's really good clinical evidence coming out now with ketones and heart failure, like they're going into heart failure patients and seeing these consistent changes in function.

And so whether it, so I'm not quite sure whether it's gonna be like myocardial infarction and like heart attack, that kind of acute setting or whether it's gonna be like long-term heart failure patients. But I think I'm, I think and it makes sense. It just makes so much sense that we think about the evolutionary function of ketones.

As this, like fuel to keep our essential organs, like our brain and our heart going during salvation, so it makes sense that they're gonna be, it's gonna be good for those systems. But yeah, that, those two, I think, are really promising areas. I just think t b I I don't know enough about it, but it just seems so difficult to study and measure, like not good biomarkers and not good consensus on, whether you should use eye tracking or cognitive cognitive testing or, how you even start to ask that question.

[01:22:51] **Dr Mike T Nelson:** Yeah. And that's hard because you mentioned every concussion's a little bit different. Like you're gonna affect different parts of the brain and even Yeah. We've got generalized areas of, this part of the brain does this function, this part does that function, but it doesn't, on an individual level, doesn't always map that directly either.

So you've got a little bit of variety of how your brain's gonna wire up from one person to the next.

[01:23:13] **Dr Brianna Stubbs:** Yeah. . But it's important as we said, as well, like lots and lots of people get concussions and so yeah, to go back to your original point, it's pretty low risk, potentially big upside. Like it's not medical advice.

I'm not medical doctor, but seems to me like a sensible thing to consider.

[01:23:30] **Dr Mike T Nelson:** Yeah, and I'm sure you've heard the research on heart failure looking at the loss of metabolic flexibility in cardiac tissue. So you just become more picky with what fuels you can use, where the heart that's very metabolically flexible, it'll, it can pull lactate directly.

I think it could even pull Peru, vate, ketones, fats, like pretty much any fuel source. It's gimme, gimme, I'll use it. But then as you get more disease, like certain fuel sources start, dropping off and you get pushed more one direction than the other direction and that causes a whole host of other issues then.

Yeah.

[01:24:01] **Dr Brianna Stubbs:** Yep. That's what, and there's another reason why I think that ketones are interesting cuz if you have a typical. Small molecule, like therapeutic, it's gonna be really specific to one pathway mechanism of action by intent, right? By designing right, it's gonna bind to a specific transcription factor or a specific ion channel or a specific, it's like targeted effect as, whereas ketones have multiple fates and multiple binding partners.

They're not, not only are they a, an energy, an energetic fuel source for the cells and the body, but they're also scavenging oxygen, reactive oxygen species, modulating inflammation, modulating gene expression. That relates also to like oxidative stress. And it's just it's because it's a physiologic response to stress it makes sense that it's having this Collage effects across the body.

Like it's really, it's the, almost the opposite to a small molecule approach where it's gonna be like having a gentle touch across multiple pathways and a net effect of that could be beneficial.

[01:25:03] **Dr Mike T Nelson:** Cool. Thank you so much for all of your time and we'll probably have to have you back on at some point to talk about your actual research and aging.

I picked your brain the whole time about ketones, .

[01:25:13] **Dr Brianna Stubbs:** All my research and aging relates to ketones and like using them as an intervention and it's been a really fun evolution to go from like performance science to aging science and the Buck Institute's doing those of really cool stuff.

And I'm learning a lot and that's what makes me happy day to day working around like other like brilliant minds and that kind of thing. But yeah, this was a really fun conversation. I don't think I said anything too embarrassing.

[01:25:35] **Dr Mike T Nelson:** Hopefully no, we have to try harder to do more embarrassing stuff next time.

You can tell us some good rowing stories or something. Oh

[01:25:41] **Dr Brianna Stubbs:** yeah, there are plenty, plenty of those. Yeah. But this is great and hopefully we'll talk again.

[01:25:46] **Dr Mike T Nelson:** Yeah. And if people wanted to find you or if you maybe don't want to be found, how would they find you? Or maybe just wanna stay hidden in the lab.

[01:25:53] **Dr Brianna Stubbs:** I'm on Twitter at Brianna Stubbs. And, I share when I have publications or when I see things I'm interested in and a lot of some like content of my like one year old Labrador and oh, athletic endeavors and stuff like that. So it's, I'm not, for a little bit of time I tried to do social media and now I just like gently partake and, it's not a super big focus for me.

I think it's a big energy drain nowadays to be too on social media. So I'm there. People can reach me if they have any questions and I do my best to reply, but don't expect a lot curated content. And I'm not on any, I'm on LinkedIn, but I'm not on any of the other.

Instagram haven't made on to TikTok yet or anything like that. So that's Twitter's where to find me if people want to contact me. And that's the best place to stay up to date with the research that we're doing at the book.

[01:26:38] **Dr Mike T Nelson:** Cool. Thank you again so much for all your time and I appreciate you sharing your knowledge.

I think it was super helpful for people to learn all about the ketones and especially the different supplements because with all the hype and everything around it, it gets extremely confusing. Like ruthy fast and you know that's not



gonna stop anytime soon. And so at least I know you went pretty hardcore into the molecular weeds, but just people got, oh, there is differences between 'em.

They're not all the same. Okay. Then, I think that's

[01:27:05] **Dr Brianna Stubbs:** probably a wind that, that's the thing to take away. And once we have more information, we'll know a bit more about what the differences are. That doesn't mean that the companies seldom are gonna tell you what the differences are.

That's the thing that kind of sucks in the space cuz you know, a consumer has to be like able to listen to the conversation that we've just had and follow it all along to make a decision, an educated decision because you shouldn't have to have a PhD in metabolism. Yeah. a product, right? Yeah, there's a lot of work to be done in this space to demystify it for consumers in that little, like 30 seconds or 20 seconds that you actually get to explain it to them.

And I think space as a whole needs to get more science so that we can talk with more clarity about, if these things are different, supplements are the same or different, but it's a fun space to be in. It's growing really fast and I think there's potential for impact. We'll accept the wars and the the flaws that it has right now and hope to see it mature and develop and have an impact.

[01:28:05] **Dr Mike T Nelson:** Yeah. Awesome. Thank you so much. Really appreciate it. Yeah, have a great afternoon. Thank you.

[01:28:13] **Dr Mike T Nelson:** Thank you so much for listening to the podcast today. I really appreciate it. Huge thanks too, Dr. Brianna Stubbs for being on the podcast. She mentioned off air that this was her first podcast in, I think over a year and a half or two years. So really appreciate all of her time and knowledge over the years.

And also just real world experience, both in industry, in academia, and then also looking at them. And what is a useful framework too? So I originally chatted with her years ago, and she's definitely one of my go-to people in the role of ketones. So if you're interested in how ketones might be beneficial for you, check out the Physiologic Flexibility certification.

It opens again on March 20th, 2023. It'll be open for one. So if you want to learn how to use ketones as one of the approaches in the certification the other ones

are temperature changes such as cold water immersion and sauna pH changes. How you would go from like a zone two cardio to truly just absolutely brutal high intensity training.

The fuel systems, which one end is gonna be ketones. The other end is gonna be a paradoxically a. Carbohydrate approach. When should you consider both of those? And then also regulation of oxygen and co2. What are some techniques? Nasal breathing versus mouth breathing. Aerobic training. And how is your body regulating oxygen and carbon dioxide?

How can you leverage that to get true longevity increases and better performance as a side? All of becoming more robust, resilient slash antifragile in the process. So go to [physiologicflexibility.com](https://www.physiologicflexibility.com) for all of the information there. Huge thanks to Dr. Stubbs for being on the podcast. Again make sure to check out her information below.

She's always sharing some fun stuff from research. And thank you so much for listening to the podcast. I really appreci. Any feedback, please let me know. Leave us whatever stars you feel is appropriate, or even a very short review, goes a really long way to helping us get other guests and just better organic distribution of the podcast.

As I mentioned, right now, I'm the only person who sponsors this podcast, so the nice part is I can say whatever I want, and then the income there is generated through the sale right now of the certifi. So if you want more information, check out [physiologicflexibility.com](https://www.physiologicflexibility.com) before it opens next time.

Thank you so much, greatly appreciate it. Talk to you next week.