

Q&A - About Keto

Bryon Jaymes: If you could just line up behind the monitor... nice single file... really it would be awesome. Because I want to give you guys enough time for as many questions as you need.

Frankie: Hi, I'm Frankie Alvarez, I've been in ketosis prior for about 12 weeks. I've always kind of eat high-fat diet, low carb. I am an athlete, the stuff was pro-athlean things, but, recently my fiancée had the same thing at about eight weeks. In ketosis, pretty solid, never had any glucose problems.

I can't say I had an A1C in a while and I know it's something to look at, but my glucose started creeping up. So, 105, 110, 115, physiological insulin resistance... different pathway I guess, I've read some stuff on it. I get the signs and things in my PhD program there, so if you could go into that, what's occurring there, I'm sure there's probably other people... It's new to me... I really dove into that because I need to know for my clients and stuff.

Dr. Nally: Doing this for 10 years and checking on sugars, I have tons of patients that are diabetic. Literally about 80%, or 85% are either insulin resistant or diabetic. It's really common to see, once you are in ketosis and you're keto-adapted, the body will essentially down regulate glucose receptors at the muscle level, so that it can spare glucose for the brain.

And you actually see a slight rise in blood sugar, if you check your fasting in the morning even up to 120.

Frankie: Yes, that's exactly what we were checking...

Dr. Nally: And it freaks everybody out because they're going, "Doc, my blood sugar is up!" If you do an A1C, their A1C is from 6.2 down to 4.7 frequently.

Well, we also see a tremendous average sugar drop, but that morning cortisol spike causes the glucose go up in the morning, so after the fast you see that rise. And because you've shifted your body's fuel partitioning, you're shifting the availability of the glucose for the brain, that little section of the brain that still needs 100 grams a day, it uses ketones for the rest of the body.

So the average sugar will bump up a bit, if you cheat and you start eating carbs, even if you do a small amount, within three days it will self-correct. The way to know is to check the A1C, that's really the only way to know.

Frankie: Alright, perfect. Thank you.

Dr. Wilson: One second, you train in the morning?

Frankie: Yeah, I was incorporating that, too, so I was training fasted.

Dr. Wilson: Okay, here's the thing, if you... I mean one of the ways especially like diabetes or whatever, If you want to raise your blood glucose to a sprint right?... So one thing we found with our research... when you do... and you're a high level athlete, so if you do anything that hits high intensity just from the adrenalin itself you're going to do that.

And oftentimes, you get an anticipatory response. So, if your body is... think about like your biorhythms are going to basely adapt to when you train... we know that. If you start training at night, you'll change your hormones and everything across the day to adapt for that training session that you're doing at night.

So we actually see when we do resistance training, we do high intensity training you will see that spike. And it could be anticipating.

Frankie: That was exactly what I was doing when I was doing the intensity sprint work, things like that. So, okay, thanks.

Physician: Hi everyone, thanks for being here, I am a physician from Canada, I also have been eating this way for a while, I personally do crossfit as well, so, the question's regarding... I know this study recently with 31 people who cross fit.

They showed great improvements but performance remained the same for the standard diet. So, I'm going to talk to my cohorts when I get back and give a presentation. But I just heard the other people discuss some of the improvements in performance.

What I was going to ask is anyone else seeing any performance improvements from doing this aside from all of the great things that come along with just being in ketosis, especially with resistance trained athletes or cross fit aside from the endurance, you know, that Volek has shown, the endurance improvements.

Dr. Wilson: I think the biggest scene that we're always seeing about these studies is this... If you look at the study that like Dom and Ryan and I and Jordan just published, these people have been eating carbs their entire life.

So, we adapted them for two weeks, and then we trained them, you know, for about two months. They gained an equal amount of lean mass, and equal amount in strength as the other group. But think about this whole adaptation and Dom can speak about adaptation like... that's only a few weeks of adaptation, they are still making those games.

So what we really need to start doing is taking people who are like you, a lot of people who had been keto-adapted for years and then put them head to head against a carb group and see really what happens then.

Annie: Hey guys, how are you? I'm Annie from Orange County. Nice to see a woman on the panel I think we need a few more. No offense, guys! I have only sons, I would like to even out the estrogen.

My question, I actually asked Dr. Nally a little bit earlier and maybe Dr. Dom can help too and you, guys. I have a family member who has what... originally was narcolepsy, but it's really is more of a cataplexy.

And so I've been trying to encourage them and he did that test, you know where you walk and you hit the wall first with your belly, so it's pretty obvious what nutritional state he's in, but you know the doctors are at a loss for what it might be and I'm really encouraging him, because I remember you saying like so many of the neurological things are metabolic in origin.

So I wondered if you had any experience, anything you could refer me to... any ideas about that, and also I want to get in touch with the guy that works with you that did all the type-1 stuff, I'd love to be able to do that because my son is a type 1 and my son is a Marine.

Hey, now you know everything about me. Thank you.

Dr. D'Agostino: Well it would be important to know if he had a sleep test, if he's had obstructive sleep apnea... You said he's pretty large, so, you'd want to look for OSA and maybe central sleep apnea contributing to narcolepsy. Does he take anything like Provigil for the narcolepsy or any kind of drugs--?

Annie: I think they've ruled out narcolepsy, they started with it but it's more of the cataplexy. So the loss of the muscle and he has his falls, where he has to sit down for a little while and then comes back. I know he had a ton of tests, I'm not sure what he's on, but how hard should I push for that?

Dr. D'Agostino: So, your question is, "Is it metabolic in origin?"

Annie: Is it worthwhile to put everything on the line and just say, you know... because I was saying to Dr. Nally that he did it for a short time, but then some kidney function were showing up to be bad and I'm thinking... "Well, I don't know what you did." But is it worthwhile to pursue a ketogenic diet for him?

Dr. D'Agostino: It can't hurt.

Annie: Okay, but you don't have anything that you've ever heard of, or could refer me to?

Dr. D'Agostino: Oh, narcolepsy, yeah. I think the diets help for that. Two people contacted me, one person used Provigil for a long time and completely got off cold turkey and he's using a ketogenic diet and has not to get back on. So, it's helping her and one other person.

But yeah, I don't know, it's kind of tough, it's not really my area of expertise.

Annie: Still you came across it.

Dr. D'Agostino: Yeah.

Annie: Alright, thank you.

Jay: Hi, my name is Jay from San Diego, and I'm wondering if there's any studies done that you know of about reversing arterial sclerosis with a ketogenic diet and/or endogenous ketones, reversing plaque buildup?

Dr. Nally: There's the Shai study which was done, they did carotid-intima thickness testing and they showed regression of carotid-intima thickness after two years on a ketogenic diet, they measured caloric restricted Mediterranean and low carb diet.

Now the low-carb diet followed the Atkins protocol, so, they reintroduced carbs back to those patients after a while, but when they did the test and they showed regression in carotid-intima thickness test.

I do carotid-intima's in my office on patients over 65 all the time and I've got multiple case studies showing regression, in fact one of the studies I've got, the lady that was on it... It was ketogenic diet, she was pre-diabetic with an A1c of 6.1, dropped at A1c to about 5.2 after the second year, and had a 19% regression in the actual plaque in the carotid intima and I've got multiple patients with varying degree of regression that way.

Now again those were just case studies, they're not any more than that, but the Shai study is the one I can point you to.

Jay: Thank you.

Abby: Hi, I'm Abby from Miami, High Tampa. I love this, thank you all so much. I'm coming from a vegan macrobiotic for 25 years, I crossed the line. Thank you, I was exercising my fitbit. I have

a severe case of osteoporosis, so I want to talk about osteoporosis, the no. 1 exercise planks or something for strength and also sleep.

I've been doing this for one year and I absolutely love this, I'm never hungry, I love it. I'm wondering with your experience in osteoporosis, can I expect without any medication any bone growth to come back?

I did 40 marathons, 20 years ago and it did not help my osteoporosis or perhaps it kept it away. Today, I ran that race this morning because of this diet, I'm coming back, I have more energy than ever. I'm having four hours of sleep it's because of this, it's not a problem, I love this diet... osteoporosis, will it get better? Is sleep important for recovery?

And just a little bonus question - one exercise for strength? Plank, burpees, anything. Somebody?

Dr. Nally: So again, I see osteoporosis all day long. In Arizona, where there's absolutely no sun, a third of the people that we see in the office that come in following a caloric restricted diet or low fat diet are vitamin D deficient and there's a huge amount of osteoporosis that we see in the population that I have in my practice.

The first thing that happens when we put them on ketogenic diet is I see about 80% of the time vitamin D self-corrects. I don't have to add vitamin D, it self-corrects. My opinion is that vitamin D is fat soluble vitamin, so if we put fat back in to the diet we're also putting vitamin D back in the diet which we've taken out in a lot of those cases.

Once you put the vitamin D in and you got calciums and magnesium, so it's all balanced if you're doing adequate exercise then I actually see improvement in osteopenia and osteoporosis. Now will it correct totally? Not in every case.

Abby: How long will that take... about?

Dr. Nally: I see improvement to varying degrees... in my office because it's all insurance based we're only allowed to check DEXA scans every two years, but every two years, I see improvement in bone density.

Now, not all people get back to normal, but I see a halting at first of that decline, that's the big key you don't want the bone marrow density to drop, you want it to halt.

Abby: Right, and what about sleep? Is somebody asleep? Is it important for recovery?

Dr. Wilson: Like the talk earlier, sleep is extremely important for recovery, like for cognitive function, athletic performance, everything. So, yes sleep is very important. Again, when you sleep, blackout curtains, turn you phone to silent, you know, when you hear a text, lock your phone in the middle of the night, all that stuff.

And actually what works really well for sleep and Ryan and I do this blocking blue light, like with the orange glasses before bed so you know, I'm sure that guys like us we are still typing and reading... And finally, remember your bones, like your muscles they adapt specific to the load.

So if it's almost like we're saying, "Well what's can be good for bone for muscle mass, for my legs? Is it going to be bench press?" No, because that's not specific to my legs. So, wherever you want the bone rebuilt, the exercise you'll have to select. So, really full load the full body you should do resistance training like a full body workout twice a week, is what I would say.

Bryon Jaymes: And I can even add a little bit to that, you know, you've probably done testing too. But sometime under tension type of workout, so if you're using your body weight or a modified pushup or an air squat, but this time you got to go five seconds up, and five seconds down for about 70 seconds, therefore stimulating your muscle fibers, therefore using a lot less momentum, so you notice some better strength that way.

Abby: So, Jack LaLanne and his juice, we don't talk about. Thank you all, thank you very much. I appreciate it.

Dr. Nally: Juice is a swear word in my office.

Sarah: Hi! My name is Sarah Quank, I'm from Denver. I'm a dietician and I'm also a type 1 diabetic. So, a question to those of you who talked a lot about this supplementation, you know you say that when these people are taking ketone supplementation, blood sugars go down and we see that a lot with like the ketonic's talk, it's a correlation that we see all the time with blood sugars and ketone production, however I'm wondering what the mechanism is behind that?

And if someone like me who is type I, and I know there are quite a few others here who are. Is that broken, I guess, because we're not making our own insulin? Would you still get those effects of keto supplementation without producing our own insulin?

Dr. D'Agostino: That's a really good question. We haven't answered that yet. My speculation is that ketone supplementation may cause not only one thing, but maybe a multiple things. So, increase insulin sensitivity, there's a review written about that by Dr. Veech, Richard Veech.

We know that we regulate our own ketone production, through various mechanisms, there's ketone urea, we pee our ketones and then as our ketone levels get elevated to a certain point, there is ketone-induced release of insulin. So, if ketones get too high, they cause a small amount of insulin to be released and that insulin can shut off or turn down our liver's production of ketones, and it's a very fine tuned balance there.

So, without your body's ability to make insulin that may answer the question as to insulin resistance or hepatic gluconeogenesis, and we think that exogenous ketones may be shifting

redox or certain types of exogenous ketones, like we know 1, 3-Butanediol, it's a type of ketogenic agent, can influence liver metabolism in a way that reduces hepatic gluconeogenesis, and it's a diol, so it has properties related to glycols, which are like alcohols.

And there's something called alcoholic keto acidosis. If you fasted for a long time and drink a lot of alcohol, you can go to alcoholic ketoacidosis and what that's resulting from is that the alcohol is inhibiting the liver's gluconeogenic capacity, so you have runaway ketogenesis.

And the same could be happening with certain types of ketone esters but we see it even with ketones that don't have this diol or glycol like component to them. So the ketones themselves and even medium chain triglycerides, if you can tolerate and take enough of it you see a decrease in glucose levels. So there's something about insulin signaling, impacting glucose levels.

Sarah: So in theory--

Dr. D'Agostino: But for a type 1 diabetic yeah, it's--

Sarah: So, to kind of correlate that then with the management for a type 1 because doing a ketogenic or a very low carb, you know, we now have to start covering protein because of the gluconeogenesis.

Dr. D'Agostino: Yeah.

Sarah: So you still have to take insulin, it's not like you can completely go off of insulin, because of the gluconeogenesis and the protein. So, in theory taking ketone supplementation would potentially decrease the need for as much insulin when you're eating protein?

Dr. D'Agostino: As much insulin when you're eating protein... maybe, yeah!

Sarah: Like if it's creating the fact that your liver isn't producing as much glucose from protein then you can potentially reduce the insulin dose? Does that make sense?

Dr. D'Agostino: I think so. I mean if you're supplying ketones and you would have a less demand for glucose, you wouldn't be... Gluconeogenic pathways wouldn't be as robust and I think that's when we're fasting, that's part of the proposed mechanism why ketones are anti-catabolic, but our brain is like a small percentage of our body like you know 3% - 4% or something, but it sucks up like 20% of the energy and a lot of the gluconeogenesis is liberating gluconeogenic amino acids from skeletal muscle to make that glucose, to ensure that we have steady fuel flow to the brain.

And if we supply exogenous ketones, that could, would at least attenuate that process and have an anti-catabolic effect. But that question about-- we have a type 1 diabetic in our lab, and maybe we can dose him up with ketones and look at...

Sarah: That would be cool. Thank you.

Dr. Nally: One other pathway may be the mono carboxylic acid is stimulated and those receptors are actually up regulated, so you actually see more of them. So the body is more efficient at using ketones over a period of time, so the need for glucose actually drops even further.

Sunny: Hi, my name is Sunny, and I'm from Utah. I'm an RN and I've got a sister in law that is a paramedic that started the ketogenic diet and what she's finding is that for the first... so if she falls off the wagon and wants to restart or has trouble staying on the diet for whatever reason, there's a period where she feels like that she's not as alert.

People on the Internet talk about it like "Keto Fog". These exogenous ketone supplements, do those help with that? Do we know?

Dr. D'Agostino: I think they do, we just haven't tested that experimentally, but the data that I showed in my talk, when it comes to the brain being able to use ketones for fuel, there's good evidence that you don't need to be keto-adapted to do that. And when we did our first study with a ketone ester, the experimental plan was to give it for at least a week and then do, but it was expensive and we didn't have enough of it, so I just had a little vial.

So it was like, "Let's give it once and see what happens." So, when we dosed it, it had remarkably seizure protection in just 30 minutes of animals that have been adapted to a high carbohydrate diet their entire lives.

So, this Keto Fog that you're talking about may be sort of the absence of ketones as if you went off the wagon you've replenished your liver glycogen and you're probably using that and probably not sufficiently at the state where you can transition back into ketosis very rapidly, so your brain may be going through glucose withdrawal and you may have low ketone levels and that may be contributing to that, and an exogenous ketone product may be able to fill in the gap.

And I think it does for me, I mean I've done that occasionally, I don't go off the wagon too much but when I do, I only use exogenous ketones and I do feel like...

Sunny: It's cool, thank you.

Dr. Nally: I'm highly insulin resistant, so I would flux between a ketone level of 0.3 and 0.7 on and off so if I am in an office and that's very stressful, and the drug rep brought in a really crappy lunch, you know, high in carbs and lots of protein on it and no fat my ketones would drop to 0.2 or sometimes even to 0.1, if I overdo the protein.

So, that's been a big challenge for me. What I found personally is that using exogenous ketones pushes me back to up 7, up to 1.2 within 60 seconds or even 60 minutes, which is fantastic. And so the fog is gone, I'm back on track and I feel fantastic. So that's the personal experience. I have a number of patients that had the same experience. For those of us that are so sensitive and so insulin resistant that really plays a big role.

Sunny: Thank you, thank you very much.

Christo: Hey guys I'm Christo, I'm a trainer and nutrition coach and I'm really ecstatic being here around you guys, because I can learn a lot. So, I do train a lot of people to lose fat along with that they have a lot of conditions with diabetes and high blood pressure, but my question is this, "What's your take on detoxes and cleanses? At some point do we need them?"

The other one is, "What's your take also on protein and acidity in cancer?" And last one is, "How do I help my clients adapt to a ketogenic diet, meaning do you have any direction as far as resources, tools, strategies, so I can slowly shift them to that direction? Let it lower it, but..."

Dr. Poff: Also with the cancer question it's an interesting question, certainly in the tumor microenvironment acidity there promotes cancer progression. The question is some kind of eating a diet that makes your blood more acidic, you know the idea... Is that going to have an effect on the tumor?

I think you know blood pH is really tightly regulated on a systemic level and I haven't really seen evidence that really support that claim, but on the other hand actually there is some interesting data showing that something that would neutralize or make blood pH a little bit alkaline... it was baking soda actually... It was some data out of Moffitt Cancer Center. They had some interesting results in an animal model that showed some effects, so it's possible, but I'm very hesitant to say that those claims are really been...

Christo: So, there's no studies that protein will make the body acidic?

Dr. Poff: Oh, that question I don't know. I'm just saying with cancer specifically... Maybe someone else I'm sure could answer that, but I mean we have a very good blood buffering system that keeps your pH very tightly regulated. So, I'm very skeptical of that hypothesis.

Dr. D'Agostino: Amino acids from proteins are good buffers, too. So, not that I know of...

Christo: As far as detoxes my take is that it's not worth it going that direction, but...

Dr. Nally: I deal with hundreds of patients who come in and bring me there colon cleanses and their liver cleanses and all sorts of stuff and I tell you all they do is raise liver enzymes. Your liver

and your kidneys were designed to cleanse your system and when you take something to clean a system that cleans the system, it doesn't make scientific sense.

I do see injury and damage from them in some cases. So, I'm not a big fan, and when I've talked to the gastroenterologist, they actually tell me, "Hey, if you fast at least once a month it cleans out your colon better than anything they've ever seen." So, just a simple fast does a great job.

Dr. Lowery: And one of the other things with cleanses is oftentimes the reason people try and do a cleanse is because they have a ton of inflammation. So, really addressing the root of that, I mean we have plenty of evidence to show the ketogenic dieting addresses inflammation, but a lot of that stems from your gut bacteria and gut health in general, so I would say focus more on optimizing that.

First and foremost for anyone that's interested in that kind of hemisphere... We've seen a lot of talks on fasting and implementing a properly, a well-formulated ketogenic diet is going to do the trick.

Christo: So, you guys are on ketogenic diet most of you, I'm assuming. Do you have people you are putting on ketogenic diet consistently? And, how do you go about meat resistance? And I was specifically talking about my clients, how can we take them in that direction? I know you do it daily on someone.

Dr. Nally: I feel like I'm monopolizing here, I'm sorry! You know, I tell patients, "Hey, your blood sugars, your cholesterol, so this the best I have, it's what I've tried, it's what my patients use that I've seen for years. Usually I say, "I want you to have bacon, sausage, eggs and cheese for breakfast" and a guy goes, "Oh, I love you!" And his wife goes "No, no, no", because she's afraid of the fat.

It's usually the females and unfortunately that's what I find, is that there's a phobia with fat, somehow in that female mindset because of what we've done in society over the years with fat. But, what happens is the husband goes on a diet, his cholesterol normalizes in three months and she goes, "Okay, I'm going to do this, too." So it's not hard to encourage someone to have bacon and eggs for breakfast.

Christo: Thank you.

Stanley: Hello, my name is Stanley Ho and I have a sad story. My next door neighbor has bladder cancer. And I feel that maybe a ketogenic diet plus exogenous ketones, my problem is compliance, like if you tell somebody to do a diet, first thing... he had a heart attack, first thing you say is, "You got to eat bacon and butter."

You're going to get extreme resistance. So, I was thinking a low glycemic diet plus exogenous ketones and maybe deuterium depleted water could help his condition.

Dr. Poff: Yeah, I mean I think that the pre-clinical data is really encouraging about carbohydrate restriction to varying degrees in various animal models of cancer. I mean there's a lot of really encouraging data, and I think that there's a good possibility that would be the case. I know of no clinical studies on bladder cancers specifically.

There also has not been a systematic attempt to characterize what degree of carbohydrate restriction is optimal for cancer. And in the pre-clinical trials that are out there there's an assumption just based on particularly what we know about cancer and the Cell Culture studies that show that increase in glucose kind of linearly increases cancer growth and vice versa with ketones, so there's an assumption that probably a stricter diet that would induce restricted ketosis is going to be most effective, but there's not been any systematic attempt to really confirm that assumption.

Stanley: Exogenous ketones added to the diet... will that help?

Dr. Poff: We can't say that for sure, there's very little evidence on that. It's a couple of studies, but my studies are very encouraging.

Stanley: Thank you.

Mary Anne: I'm Mary Anne from the Bay area, thank you so much, every single presentation has been really valuable and I appreciate your time.

So, I'm trying to put all these together into an optimal lifestyle for good health and disease prevention. I feel like I have really good tools on the ketogenic diet, low carb diet, intermittent fasting, exogenous ketones and I was wondering if-- for someone who's clearly not high performance athlete, but athletic and trying to do those things for good health.

I have read some and heard some of you talk about strength training and such, but what I'm specifically interested in is that I've read references to, you know, aerobic activity, interval training and timing that during the fasting period. So I wondered in terms of just helping me with my overall lifestyle, if you could comment on exercise and timing of the same. Thank you.

Dr. Wilson: So, Mary Anne, your question is timing of exercise relative to the fast?

Mary Anne: Yes. And also the intensity and duration of the exercise.

Dr. Wilson: So, one of the things like always with exercise, we always do what's called a need analysis which means what are your goals, like what are your needs and that will determine the

intensity. Some people just go, a lot of times some are interested in body composition and overall health. So some people are coming to me and go--

Mary Anne: I was asking more specifically as it relates to ketogenic lifestyle like depleting glycogen. I wasn't asking from general health.

Dr. Wilson: Okay. Ryan actually... in fact do you want to tell them about your study?

Dr. Lowery: Yeah, so, we do this study, because that's kind of one of the things we want to see is how fast you can induce a state of ketosis. So, we had people kind of do high intensity in their role training. In our lab we do like really high intensity something on those wingates, so maximum output and within a week, within four days we've actually seen people elevate ketones, I think it's a great suggestion.

Oftentimes when people go into a ketogenic diet, they go "Well, I'm going to back off of my training." We actually think it should be the opposite. I think you should go full into it, into your training to try and deplete as much as possible, fight through those... the keto fog, the keto flu and induce the state of ketosis as quick as possible.

Mary Anne: And how about the timing? This would be the fasted state.

Dr. Wilson: Well, the thing is if it's relative to glycogen, so your carbohydrates are low, you're going to deplete. If you're not keto-adapted yet... assuming you're keto-adapted... I mean if you're keto-adapted for a long time like Volek showed, if you've been on a keto diet for like 18 months, you'll replenish even if you start eating fat.

So, if you're already adapted, then in that case, I think the time is more of a move point to me. There was a research with the Ramadan, there were a lot of intermittent fasting researches... They restrict feeding and then exercise studies and the timing of the exercise didn't matter as much, but I would say is this, what we do think as far as recovery, if you're interested in recovery since you're already adapted, it's far better to time it around when you're going to have protein after. If you're interested in repairing.

Particularly, there's some research with aging and muscle in sarcopenia, that timing does become important with aging. People will question it when people are like super young and everything works for them no matter what they do, but after the age of 50, there is some research that indicates that timing and exercise is relative to any other protein-containing meal, and could be important. So, our time to exercise is relative to when you're going to eat.

Stacey: Good evening, my name is Stacey and I'm from Toronto. I'm here with a group of folks. We all have McArdle's disease. Does it ring a bell for anybody? So, the really quick elevator speech of what McArdle's is, is we can't access stored glycogen in the muscle.

So there's a really unique phenomenon called Second Wind, whereby we can utilize blood glucose and free-fatty acids as a source of energy for any aerobic based activities. So, the question that I have for whoever wants to answer is, "What do you think the role of the exogenous ketones would be for this patient population?"

Because one of the concerns is of course acute muscle breakdown, Rhabdomyolysis, compartment syndrome and potentially acute renal failure. So, you know the thinking... perhaps a lot have tried a ketogenic diet and have had success not having to wait until that Second Wind, but I'm wondering if exogenous ketones would help further alleviate that time period?

Dr. D'Agostino: Yeah, it would make sense to me based on what I know that if you shift your metabolic physiology away from using glucose, which is dependent on glycogen breakdown, which is impaired and shift your body more towards fatty acid and ketone utilization that would be preferable. And we know the body is incredibly sort of plastic and adaptable to allow us to do that and there's a number of metabolic adaptations that allow us to do that.

And I think ketones would help to, would be beneficial for that process because you would be supplying an alternative energy substrate that is independent from glucose that would sustain energy metabolism and I know there's at least one study on glycogen synthase disorder that used sodium beta-hydroxybutyrate infusions along with I think a modified Atkins or a ketogenic diet with good success.

I think there are already some data there to suggest that it would. If you just get on Pubmed and look it up, it should come up because--

Stacey: It was one patient.

Dr. D'Agostino: Was it a single case? I thought it was...

Stacey: It's unfortunately a rare disease, you end up with this very small--

Dr. D'Agostino: Yeah. I thought it was a couple, but... I think there's some suggested evidence, based on what I know on the basic science and from a little bit of clinical data that it would be helpful and you know exogenous ketones didn't exist commercially, you know just a few years ago.

So, now we potentially have this tool and I think it would be important to study this disease specifically and perhaps study a range of different types of exogenous ketones to see how therapeutically would work perhaps in an animal model first and that would be the pre-clinical data could set up to prove of concept to do a clinical trial. So, which is something, you know, I've actually recently been looking into maybe doing that.

Stacey: Perfect, thank you so much.

Dr. Lowery: One thing real quick... That is actually Dr. Veech's brand new study that he just did. Actually shows that they're actually recommending that ketones are the preferred fuel source over fat and carbohydrates first and foremost. So, they looked at glycolytic intermediates and you actually see a sparing of glycolytic intermediates when exogenous ketones are given.

So like Dr. Dom said, it would absolutely make sense.

Dr. Nally: The other thing is that when you increase the ketones over a period of time you're actually up regulate all of the MCT transport system, so your ability to clear lactate really improves, so the likelihood of ...

Elaine: Hi, I'm Elaine, I'm local, I've tried to have some family members adapt to a ketogenic diet and one of the motto's I think really doesn't help the shift in behavior change is moderation in everything. And so people think, "Oh well, it's just one little piece of food or one bag of potato chips or something like that."

And, I think something that would be helpful in the adoption of this change in your diet is something like they did in this anti-smoking realm which is to say, you know, one cigarette will take three minutes off your life. So, I think a place where clinic could meet with research is to know that like that one bag of potato chips is going to ruin one mileage, like it's going to cause some kind of a nerve damage or you know some kind of organ damage or something like that.

So, any thoughts that you might have along those lines to give a visual to what falling off the wagon does to you and leads to complications of, you know, glucose.

Dr. Wilson: So, you know the saying like, "Yeah, you have your cake and eat it, too?" It's kind of what you're asking. Quest Nutrition is actually the company that's doing like... They're one of the biggest fear ads on this. They're obviously coming out with products words like CheatClean. They have potato chips, they have stuff that tastes like carbs or honestly their peanut butter cups are better than the real thing, you know what I mean?

So, it's like you're having that, but you're still staying in ketosis. So, I think it's really like seeking out alternatives, but the other thing is like, if you had a potato chip, it's not end of the world. I do think exogenous ketones like Dom said, you know, there are times like when family members come in and ask maybe some sushi or something like that. If you're highly adapted, you get back pretty quick...

Bryon Jaymes: And I can help with this too. You need to make sure that they're following Dr. Jacob on Instagram, because when you see some of the foods that he posts, their mouth will water... I mean I envy the things that you create as alternatives. So, seriously following him on

social media, because he pose all the ingredients, everything to do... He made this cookie one time that was just... I stopped everything and went right to the store...

Dr. Wilson: I really appreciate it, it's like the Muscle PhD. I just flagged it, but seeking out alternatives like Quest bars, Quest Nutrition chips and stuff and then Muscle PhD.

Bryon Jaymes: Hey, one more time - that's Muscle PhD.

Steven: Good evening, thank you for being here. My name is Steven, I'm from Pluto. That way out. It's still a planet? Because I know that when I talk about high-fat low-carb, I'm also a retired marine.

Bryon Jaymes: Hurrah!

Steven: 27 and a half years in retirement, still alive. You mentioned Dr. Veech a couple of times and depending on how you look at it, I listened to a very disturbing or enlightening podcast he did with Dr. Ben Greenfield. You know where I'm going with this, right?

As is the case with most things, we have awesome lifestyle and there's people trying to exploit our lifestyle by you know, presenting us with alternatives, you know exogenous ketones that may or may not be. I don't understand the racemic and the redundance and all of that, I'm just trying to make an informed, intelligent decision if I'm going to spend my hard earned bucks, retire dollars, on exogenous ketones... is it the right one for me?

I mean, I know I got to make that decision, but when you look at the science, there seems to be some very conflicting science concerning this specifically. Any thoughts? Depending who you listen to... some guys like the guy, you know he's 46 years and he invented the modern ester ketone, and other say is a quack, I don't know.

Dr. D'Agostino: No, he is not a quack... Dr. Veech was actually a really big mentor to me. He is one of the first people that I reached out to, and I would actually say he is a leading authority on his ketone ester, which is the R Enantiomer, you have to keep in mind that he's been working on this for over two decades and has a lot of money, you know, DARPA, well over \$10 million invested into that specific ketone ester.

So, other ketone technologies that emerged are in competition with that. And I think he believes that his particular ketone ester is superior to everything that's out there. The data doesn't support that though, so that's his opinion and I think it's an educated opinion.

But, the data... When we did our studies for oxygen toxicity, one of the first esters that we used was the R Enantiomer of beta-hydroxybutyrate and it didn't work for CNS oxygen toxicity. And if you saw my study, it's because we also needed a boost in acetoacetate.

So, I collaborated with Case Western, Henri Brunengraber who was Dr. Veech's colleague and actually superior knowledge in global metabolomics and it's really the leading. He runs an NIH sponsored metabolomics core facility there. And he essentially gave me a recipe to make an ester that elevated both beta-hydroxybutyrate and acetoacetate. It was racemic and it worked remarkably well.

And then, we went on to work with different chemists, to develop, you know, racemic beta-hydroxybutyrate salts and they have what appears to be remarkable therapeutic properties. I've been on expert panels where I'm on a review committee to look at all the data on the racemic and there was no data that indicate that they are dangerous in any way.

And there are actually prescriptions for different types of metabolic disorders. And actually I have a whole file study, showing their therapeutic efficacy in a wide range of disorders, so, I would say that the ketones that are out there now, the racemic that beta-hydroxybutyrate as part of the ketone salts are very effective, they probably will be cheaper as time goes on, as they scale up production.

And also keep in mind that Dr. Veech had mentioned that the R Enantiomer is the natural form, but the L is also natural. We have L beta-hydroxybutyrate dehydrogenase enzyme that occurs naturally, it's a natural enzyme.

So, there's an enzyme that interconverts the two Enantiomers that are found. So when we consumed either one, they are metabolized, sort of naturally in our body for energy metabolism.

It could be that the R Enantiomer is superior in some ways and we think the L Enantiomer which is the other hand, the mirror image of it, also has therapeutic properties that may not be seen with the R and that it can lower blood glucose levels.

And that's been shown in other labs. So, it's a long answer to your question. I don't think they're dangerous and that's the first and foremost and I do think there's evidence there, that they're very therapeutic.

Steven: Can we sum it up, and say it's like halitosis taking exogenous ketones better than no breath at all?

Dr. D'Agostino: So, you're asking, should you be spending your money? I think that's a personal decision.

Steven: Well, yeah, of course. But would any of the high grade... because I'm not Thelma, Selma... some serious pharmacy... But, exogenous ketones, they're helpful, I mean, like halitosis, better than nothing at all.

Dr. D'Agostino: We're all fans of the ketogenic diet as a way to elevate our ketone levels and MCT oil.

Steven: I'm totally ketogenic, but, I mean, just to get that little extra boost, you know.

Dr. D'Agostino: Yeah, yeah without a doubt, I think there are benefits to further boosting your ketones and if exogenous ketones are a way to do it, as is MCT oil, the C8 is actually remarkably effective and the combination of the salts and the MCT together is really what we tested.

And I think they are reasonably, you know, inexpensive, I mean if you just want to use them... I don't use them every day, I didn't use them today, but I do use them a couple of times a week and I think, it's worth the money to me.

Steven: Thank you, thank you very much.

Melanie: Hey guys, how are you? You did an awesome job today, by the way. I said guys, so I wanted to make sure I say girl. Okay, so my name is Melanie Miller, I'm from West Virginia, I've lost 85 pounds in the last 11 months. Yeah.

Thanks to the legendary Dr. Eric Westman, I started his program. And so this is my big question now. I've actually helped over 6,000 people in the last 8 months get on the hill program as well and they've begun to lose weight. But here's the problem, I had a trimalleolar brake in my right leg.

I was a runner prior, that's how I gained the 100 pounds, because I started taking pain pills and decided to eat sugar and thank goodness, I had another physician tell me about them. But the problem now, is I've lost all this weight, I can't run, but I want to work out, I want to do something.

I haven't worked out, I walk occasionally, but I just need help. I've gone online and the question I get, thousands of questions and one of the biggest questions they always ask me is, "Melanie, is the skin going to ever get back to normal?"

So I need some doctors to be real with me, this is the moment of truth. I need to know that and then if there's a program that you guys tell your patients about, so that I can help others, you know, begin to get to move. That's the biggest thing for me right now and that's where I'm stuck.

Dr. Nally: I have multiple patients that have lost over 100 pounds and the skin remodels, it's just slow. You are your own plastic surgeon and it will come off as fast as it went on. The challenges, and that's one of the reasons I tell patients, In your first three months, you're going

to lose a bunch of weight, you'll lose 5 to 15 pounds in the first three months, then it will slow down.

Then that weight loss will slow to 2 to 5 pounds per month, at least in my practice. And that's I assume, because the skin is remodeling, otherwise you'll look like the Michelin Man with a bunch of rolls of skin. But you don't, and all of my patients come in and they'll have pants that two people can get into. And the skin is remodeled, it does, it just takes time.

And I think the amazing thing is that, when you're in ketosis, the inflammatory improvement that you have, allows the skin to improve, that tends will affect the skin and actually improves. It's the closest to the fountain of youth that we have, because it actually slows those free radical formation and it actually improves that.

Melanie: So, then it will. There's hope for me then without surgery? That's what I needed to know, thank you so much.

Hello, I would have expected that there would be more questions on epilepsy and cancer, but I think those presentations were, you know, just so good that I don't think there were many questions left unanswered. My question is no different from the other ones; it's regarding exercise and insulin resistance, horrible insulin resistance.

So, I guess mostly it's for you, but if anybody else has something to say... Three years ago, I read a couple of scientific studies that mentioned that the best way to get your body to be sensitive to insulin again, would be aerobic exercise at the top of your capability for 30 minutes. And I think it had to do with glycogen depletion and replenishment or whatever that type of process.

And it talked about how aerobic exercise will be much better for that than for example, strength training or yoga. And would you happen to know if that is true? I have tried to find more information on that topic and I haven't found very much. So, what would be your take on that?

Dr. Nally: From a clinical perspective I see the resistance training is the most effective. Either they hit training or you're doing intervals or resistance, seems to be more effective in improving the insulin resistance and at least that's the studies that I've seen.

Dr. Wilson: Yeah, so, the biggest thing is yes, to answer to your question, yes, it is tied to glycogen. So, if you look at people who are insulin resistant, type 2 diabetics, overweight... oftentimes they are sedentary, so, it's a combination of the Western diet, like McDonald's and stuff like that, combined with a sedentary lifestyle.

So, the best way to think about is like, think of your muscles as having sort of a fuel gauge inside of them, so, think of the fuel gauge being like full, empty, full, empty. So, if you have low activity

and then high amounts of carbohydrates at the same time, lots of energy... the system is always full.

But what happens when it gets empty? When it gets empty, it turns on a fuel gauge-- You guys all know ATP? Everybody knows ATP, right? Okay, so, an ATP gets broken down, it gets broken down to AMP and so that turns on the fuel gauge and basically your cells goes "Oh, I'm out of energy, I need to create more mitochondria".

And the more mitochondria you have, the more insulin insensitive you become. So, insulin resistance in large parts it's like a metabolic disease. So I think, now, as far as when you say 30 minutes, here's the thing, if it's tied to glycogen depletion, I could deplete glycogen in three hours by going very slow and low, and that could be fine, that may be someone's preference.

But there is data that show that if I do all out sprint, everything I have, I can deplete in 30 seconds time, I'm going to deplete almost 30% of my muscle glycogen, any given muscle group. 30 second, 3 hours. So it really comes down to your decision, the higher the intensity is, the quicker those adaptations will happen.

So it's all about your preference. So that's going to increase the mitochondria, but then remember, muscle is one of the largest depots of carbohydrates. So, we are talking about glucose tolerance beyond the store carbohydrates, having more muscle, is going to also contribute to the store with more carbohydrates.

So the combination of aerobic and resistance exercise is going to be important, depletion of glycogen and more of a depot, more muscle mass, to store carbohydrates is a great tool. Okay. So, select what you like.

Alright, thank you.

Dr. Wilson: You're welcome.
