

Paleo Solution - 393

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Robb: Hey, folks, welcome back to another edition of the Paleo Solution Podcast. Robb Wolf here. Today's show is awesome, just super exciting. I think I've mentioned to you folks that I'm about 20 years into this Paleo low carb ancestral health kind of exploration and I honestly never thought I would live to see the day that a company like Virta Health and a doctor like Dr. Sarah Hallberg would happen.

If you're not familiar with Virta, they are a company that was formed by Drs. Phinney and Volek, famous within the ketogenic diet realm, and also Sami Inkinen who is kind of a luminary in the tech startup scene. They had this kind of wacky idea that maybe using a low carb ketogenic diet could be incredibly powerful in stemming the tide of the type II diabetes epidemic that all industrialized nations face.

And so Dr. Hallberg is a key player in this story, an amazing clinician, really a fascinating back story as to how she came into doing what she's doing. She was a high carb low fat Dean Ornish advocate and then when she started really reading the literature and digging in on what should work and wouldn't work for the problems that she was seeing in a clinical setting, that high carb low fat vegan based diet just wasn't really cutting it.

So she iteratively moved towards a lower carb approach and now is involved with Virta Health. We got to dig into a lot of different topics. We unpacked the recent study that Virta published on a year-long intervention with 500 folks on a ketogenic diet. We talked a little bit about where people can go awry in chasing ketone levels. Clearly, ketones are important signaling molecules. There's some efficacy to having some degree of ketone levels.

I personally, when you look at in the internet, you see a lot of people running around by chasing specific ketone levels. They will do squirly things like really restrict protein, elevate fat, and start actually gaining weight on a ketogenic diet. And so it was great to talk to Dr. Hallberg and kind of unpack her experience around that. The real takeaway was that although we have this big picture ketogenic diet concept we really need to lean heavily on personalized nutrition, which is exactly what they do with their team of health coaches leveraged with a technology platform and then integrating with their primary health care providers.

I think you're going to really enjoy the show. If you see folks or you know folks that are struggling to succeed with the ketogenic diet, drive them towards this episode. Point them out to Ketogains bootcamp or drive them towards the Keto Masterclass, robbwolf.com/km, and we can help save a lot of folks. So, dig in and enjoy the show.

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Hey, folks, I am here with Dr. Sarah Hallberg of Virta Health. Doc, how are you doing?

Sarah: I'm doing great. Thanks so much for having me, Robb. It's great to be here.

Robb: Awesome. Well, I was so excited to talk to you that we started jabbering like 600 words a minute and then it occurred to me, well, she'd probably record this on the podcast. You actually have one of my dearest friends, one of the directors the Reno Risk Assessment Program, Dr. Jim Greenwald a.k.a. Greenie, you've got him in town with you. You have your chief of police and all kinds of exciting things going on there in your brick and mortar setting. But what else is going on with you?

Sarah: Wow, so much. I mean, Robb, I don't have to tell you or convince you that this is a great time to be in this field and in this space because so much is happening right now and you really can just feel the momentum building for some major change that, of course, at the end of the day is going to help the patients and the people that we care about.

I'm just so thrilled to be part of that movement. Again, I just think that we're going to have quality of life improvement and longevity improvement for so many people. So, to start off with what's going on, we just published a paper and that is the one-year results of our very large clinical trial looking at a nutritional ketosis supported with telemedicine at reversing and treating type II diabetes.

We are about to publish our one year cardiovascular risk assessment in that same population and have just recently submitted a paper looking at outcomes on fatty liver disease. So, lots going on in the research world. Of course, in the non-research world, Virta is doing very well. And you may have heard but we just had our series B round of funding for 45 million.

Robb: Congratulations.

Sarah: Thank you.

Robb: That's pretty awesome, yes.

Sarah: Just really shows that there's a lot of faith in the company to be able to be a major player in what has really become the country's leading epidemic which is, of course, type II diabetes followed by obesity.

Robb: Which are all intimately related in so many of the other comorbidities, co-mortality issues that we face ranging from neurodegenerative diseases, autoimmune disease, a host of different cancers, all clearly have a metabolic underpinning. And so if we kind of get out in front of this kind of diabetes related issue we are by extension tackling a whole host of other problems simultaneously.

Sarah: That's right. And, of course, so this can lead to health improvements, as you pointed out on many fronts. And then we have to go back to what also can this save us financially which is a factor. Of course, pales in comparison to improving the health and the lives of our patients, but at some point the money does matter as well because most people already know diabetes is breaking us economically as well.

Robb: Yeah. We chatted about that a little bit before we started recording. People are not really aware that some very nonpartisan government entities like the Congressional Budget Office, they're about as vanilla and unpolitically affiliated in entities you could find within a governmental agency and these folks' predictions 2030, 2035 that essentially the US is bankrupt and solvent, however you want to call it, due to diabetes related issues alone.

We were also chatting a little bit like there's really this kind of watershed moment where folks like chiefs of police and mayors of cities and whatnot are getting in and championing this kind of ancestral health low carb approach to dealing with this problem because we've had a good 50 or 60 years of standard of care high carb low fat, eat less move more, and it just flat hasn't worked.

I think that shell game is really kind of winding down and coming to an end and the pointy stick of economic collapse is actually pushing people into doing something new. But, Doc, I'm so curious. Another bit that I mentioned before we started recording was that I literally wasn't sure if I would ever see an organization like Virta, a doctor like you championing this stuff in my lifetime.

This is now March, year of 2018, tinkering with low carb ketogenic Paleo type diets. How did you get involved with this and what was the process of going from a standard of care trained physician and then transitioning into the spot that you're at now?

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Sarah: Well, actually, lots of pivots. I always like to say, my advice to people in getting started is when you're talking about your career, when pivots occur, welcome them because they can lead to some of the most exciting career moves and opportunities possible. And my career looking back is filled with some really important pivots.

First of all, I actually did not grow up thinking I was going to be a doctor. I was an exercise physiologist and I was in the middle of getting my masters degree and also working in cardiac rehab at a local hospital at the same time when I had an aha moment while arguing with a cardiologist, actually. It was a fight with a cardiologist that got me into medicine because I was so frustrated because the cardiologist I was working with didn't understand anything about exercise, really weren't thinking about preventative medicine.

It was cut to the point where I really understood in working the hospital setting that if you can't beat them, join them. And that in order to be able to really make changes I was going to have to become a physician myself. I wound up going back to medical school late. The funny thing is I had just been accepted to get my PhD at Purdue University when I called my parents and said, "Hey, I'm not going to do that. I'm going to go to medical school."

I like to joke around that says I was the only doctor in the world whose parents were disappointed when she told them she was going to medical school because they were both professors. The funny thing is I wound up practicing in the Purdue community. It's just a strange occurrence. Anyway, so I went back and went to medical school with the plans of becoming a preventative cardiologist.

At that time, Robb, here is an interesting secret that I don't think I've ever really talked about before. I was Dean Ornish's number one fan. And I was an absolute low fat believer. For myself I would eat low fat. My husband and I never ate red meat. I mean, I just bought it hook, line and sinker like everyone else because this is what we are being taught in graduate school, this is what I was taught in med school.

So then I wound up, long story, had a child in med school and so decided to just stop at internal medicine residency. I never went on to the preventative cardiology route. I practiced primary care for close to a decade and in there I saw firsthand this kind of stuff wasn't working. I mean, everybody would come back just worse. I would come home and lay my head down and complain to my husband. I say, "I am a legal drug dealer. I am just part of the problem."

It was really depressing. I knew full well I wasn't going to be able to live out my life in primary care because of those facts that I couldn't escape. One day,

because of my background in exercise physiology, the administration at Indiana University Health asked me to start an obesity program. I was all in. I was like, "Absolutely. I would love to do that, get back to my preventative medicine roots."

So, essentially, this was going to be a program started from scratch. I spent literally a year with my nose in the literature looking and reading everything and completely shocked to find, wait a minute, there's no data for what we've been telling everyone. There's nothing. This low fat diet, where did we get this idea from? And clearly, there was evidence to support a low carb approach.

So, day one, our obesity clinic at IU started as a low carb clinic. So, starting the clinic was my pivot. And then the next pivot came really quickly afterwards because what we were seeing was, sure, people were losing weight and that was the original intention of the clinic, but what we were seeing that was more amazing and more impactful was diabetes was going away. Nobody told me that could happen.

We're getting people off hundreds of units of insulin, normal glucose control. Where is this written about? Where is this in the guidelines? How come we don't hear about this? And so out of frustration that, of course, you can't find this in the guidelines, I did another pivot and started doing some research.

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Because I said this is unfair. This needs to be available to everyone. Why should this be limited just to my community? And, of course, there were a couple notable exceptions. Eric Westman at Duke was already doing this and some other very forthright leaders in the field, doing it in small packets. But why is this not in the guidelines?

I teamed up with some people at the nutrition department at Purdue and did just a small unfunded pilot study where we compared patients, just direct suspected chart review of our patients versus patients treated with the dieticians using standard of care. And the results of the study, of course, showed metabolic advantages with our patients but, more importantly, at least for the IU here now was a significant cost savings.

So, I was at a conference very shortly after we completed that study. I had been starting to look for funding and who should I happen to run into at actually the obesity medicine association conference was Steve Phinney. I walked up to him and I said, "Oh my gosh, you got to hear about what we're doing in Indiana. I'm looking for funding but we've got this great program." Steve and I went out to dinner that night and it's kind of the rest is history.

He said, "I'm starting a new company. We'd love to fund your trial." Steve just about lived here in Lafayette, Indiana for a year along with a whole host of researchers and within nine months of meeting Steve Phinney we had an almost 500 patient clinical trial up running and fully enrolled at a single site which most people would think was impossible except for the fact that the research team and I didn't sleep essentially for those nine months.

Robb: Details.

Sarah: Yeah. I mean, who needs sleep when you're doing something this cool, right? And, of course, the company he was starting co-founded with Jeff Volk and Sami Inkinen was Virta. So, not very long after that, I joined the Virta team too so both worked at IU Health and also Virta and then just thrilled to play a role here. So, that study that we started right after I met Steve was a study that, again, we just published the one-year results on.

Robb: Amazing, amazing. Doc, that is fantastic. Doc, do you want to unpack some of the results of the study? I know that you guys have done several write ups for it and there's been quite a lot of buzz about the study and I know that there's lots of additional information that will come out. Like you mentioned, there will be some specific looks like the cardiovascular disease markers coming out soon. But, do you want to unpack for folks a 30,000-foot level of what we found with this study?

Sarah: Absolutely. So, just kind of quick background on the study. We enrolled, as I said, almost 500 patients. 400 of those were intervention patients and 100 were treated with the standard of care. So, all intervention patients were treated with a low carbohydrate high fat diet with the goal of inducing nutritional ketosis. Now, in addition to that, these patients were helped by, again, you said the use of telemedicine.

They were supported remotely and they all had access to an app. Through that app, they got a health coach, they had physician supervision, they were able to track their biomarkers and by biomarkers I mean track their weight daily. They got a scale that was cell phone enabled so when they step on the scale in the morning it automatically populated into their portal on the app. They were able to log their glucose and their ketones.

I'm going to come back to that later, but the ketones that we measured were serum ketones. So, again, we were able to really be able to rely on them for patient progress, patient counseling, and then I'll talk a little bit more about how they applied to research. These patients were also given access to a resource page and a patient support community online.

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So, really what we call like the five pillars of support there. Again, it's health coach, physician supervision, which is critical when having to adjust medications for someone with a diagnosis of type II diabetes, resource page, online community and then the biomarker tracking. And so through this their health coaches were able to really personalize their nutrition intervention.

Of course, everybody was restricting carbohydrates and increasing fat in their diet but we were really able to take account of things like lifestyle or is this someone who's eating in the airport on the run or is this a stay at home mom or a farmer. We were able to make changes patient by patient based on some of those things.

Of course, how they were doing? What is their blood glucose looking like? What is their ketone level looking like? I'll tell you the neat thing about this is having that almost real time access to what people's ketones and glucose were. We're able to counsel patients about what they were eating right then and there because one of the limitations in free standing clinic is that, well, when they come in and see you, even if it's once a month and you say, "Oh, hey, it looks like your glucose is trending up, what have you been eating?" It looks like -- nobody can tell you exactly what they ate two weeks ago.

But then you are getting that instant feedback from them, this is what my glucose is now, this is what my ketones are, we can say, "What was your last meal?" And we can really pinpoint it right away to something that they can remember. Okay, I remember what I have for breakfast or dinner last night or breakfast this morning. We can counsel them based on that, up-down in certain macronutrients or give them new ideas of recipes and things that they could try.

So, it's really helpful. That was the intervention patients. We followed these people. We published results on the intervention patients at 70 days and one of the things to touch on with the 70-day paper, even though it's a bit dated now, is just how quickly things happen. Patients improve dramatically in just this short 70-day window. Actually, they have lost 7% of their body weight at that point in time. Their A1C had dropped by a full point.

And for any of you listeners to have type II diabetes and so understand and follow their A1C which is a marker or lab of glucose control, a one point drop is huge. And at that point in time over 50% of our patients had reduced their blood sugar to below the threshold for diabetes just in ten weeks. And so then we followed those patients out to a year because one of the criticisms, as you well

know, is that people say, "Well, this isn't sustainable. People could do it for a little bit of time but they can't stick with it."

Excuse me. I beg to differ with you on that. Because, of course, we've had patients in the clinic successful for years but at our one year, a retention rate in the trial was 83%. That's literally unheard of in a nutrition trial. So, people were sticking with it. And what happened with their results? They got even better. Even though they have that dramatic dive at ten weeks in their blood sugar and weight it continued through the first year.

So, a year, patients lost 12% of their body weight and their A1C went down by 1.3 points. We saw other improvements too. For example, in inflammation. Markers of inflammation especially one called C reactive protein, which is a well-known and accepted marker of inflammation, dropped by 40%. I mean, again, that alone is an absolute fantastic indicator of health.

We know that that reduces cardiovascular risk. I'll tell you patients can feel that. When you say, "Hey, oh, by the way, now your inflammatory markers are normal," the first comment that I always get is, "I can feel that." So, it's just great. The liver function tests results decreased dramatically. Triglycerides dropped.

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Here's the interesting thing, people are concerned all the time. Well, this is going to raise their cholesterol. But what we saw that ApoB, which is the best predictor of cardiovascular risk especially in an insulin resistant population, did not change. So, it didn't go up. It stayed the same. At the same time, of course, from other lipoprotein standpoint, triglycerides dropped significantly.

Their HDL or good cholesterol went up by almost 20%. So, we essentially saw across the board improvements in these really important health markers and cardiovascular risk indicators. The only thing that went up was their LDLC, went up by ten points. But, again, ApoB or LDLP in this insulin resistant patient population is a much better risk predictor and that did not change.

It's true. People can dramatically improve their type II diabetes and even reverse it while maintaining excellent cardiovascular risk profile. And at a year the intervention patients, it was up to 60% of them that had reversed their type II diabetes. Meaning, they had an A1C under the diabetes threshold, off diabetes medication, with the exception of Metformin in some patients. The reason that that's an exception is that Metformin is indicated for reasons outside of type II diabetes. We actually, for the most part, encourage patients to stay with it even when their blood sugars improved.

Now, I want to contrast this to what happened with the control group, the patients treated with standard of care. Of course, over that year, they took more medicines, their weight didn't change, their A1C got slightly worse. But again, while they were taking more medications. So, we can see that the standard of care of method is not serving our patients. It's not helping them maintain their health goals.

I am so happy to be able to present results like this because one of the other things that I really hope comes out of it is we stop blaming the patients. Patients want to change. They are all in. But, of course, it's really important that you're giving them advice and asking them to do something that's actually working. And when the advice is wrong and patients don't get better we can't come back and say that it's their fault.

It breaks my heart, honestly, as a provider who sits with patients who are so frustrated all the time. I get to tell them, "It's not your fault. Let's give you some advice that not only you can stick with but you can see the results quickly and you can get sustained health improvements." It's fantastic.

Robb: It's amazing. I'm looking forward to a day when we do kind of a UFC ultimate fighting challenge type of thing and we just throw down the gauntlet and we're like, okay, standard of care medicine, you guys are going to compete against this ketogenic approach, and all the plant-based vegan, you guys are going to compete too. Whoever wins this thousand person trial, everybody else closes up shop and goes home and then we have like the dominant paradigm. Although these guys will never ever sign off on that.

At some point if you -- I think before we recorded, I made the analogy of a superior computer operating system. At some point, particularly when we're just seeing systemic failures everywhere with standard of care, this better methodology is going to push its way through. It's just incredibly exciting. Do you know off hand what the patient compliance was in that control group? I'm just curious.

Sarah: What the retention rate was in the control group?

Robb: Yeah.

Sarah: I'm sorry I can't come up with the number right off the top of my head.

Robb: No problem.

Sarah: It was reasonably high. They were continuing to stick with it. But again, it wasn't showing them success.

Robb: So, I think an interesting thing here is you guys had a matrix driven process both on the ketogenic side and on the standard of care side which involved consistent feedback, social support, integration between health coaches and primary care providers.

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Even though you guys leverage technology to affect this change, we still had what my computer programmers affectionately call meatbots, like actual living breathing people that were able to leverage their expertise with a technology interface. But both groups, being anywhere around that like 80-85% adherence to a year-long trial, that's pretty damn impressive.

So, just from a systems based approach, this matrix driven idea is really kind of a non-negotiable topic in my mind. If something is going to be successful in the future, it will have all or possibly additionally some other elements to it that look much like this. Would you agree with that?

Sarah: I would. I mean, I think that telemedicine is the way of the future. We're learning at Virta Health really early on how do you exactly make this work? How do you monitor patients appropriately and safely? And how can you use, again, just as you're saying, people on the back side, the health coach, the physicians, how do you best use their expertise to be able to personalize medicine and interventions with patients?

Because I think that personalization, it's just so key. We can say a low carb high fat diet inducing nutritional ketosis works well for patients with type II diabetes. I believe that that's pretty darn uniform. Patients with type II diabetes are going to do well on this. But that being said, that's very different from saying John Smith and John Doe are going to be doing well with the exact same approach to that because that's going to be slightly different.

How we implement these things just needs to have that personalized touch to it. And with the Virta Health and the remote care teams that we have put together, and by teams I mean, of course, the health coaches, of course the physicians, but we can't forget all the wonderful people behind the scenes, the engineers and the coders and everyone putting together the content that helps make this successful for patients. It's a team effort.

Robb: Yeah, it is, and it's a massive amount of infrastructure. It's just incredibly impressive. Doc, it's interesting because on the one hand you guys are using a

uniform and one could kind of argue a binary approach to this intervention. Are you in ketosis or not? But then at the same time you got a high degree of individual customization going on. I think that's a really important takeaway for folks when we're thinking about this, although there's kind of an overarching concept of carbohydrate restriction and a shifting towards fat as a primary fuel source and whatnot, there is oftentimes a significant amount of customization there.

In my dealings with folks on the interwebs and trying to help them navigate the story and also that we use a ketogenic diet in our clinic in addition to just low carb and Paleo approaches depending on the individual, there's definitely some controversy out there on topics like adequate ketone levels. I've noticed over the course of time that ketones tend to trend downward when folks had been ketogenic for a given period of time.

I've eaten more or less this way for the past 20 years, the last six months I do a ton of Brazilian jiu-jitsu and some other athletic endeavors and I'll range between 40 to 60 grams of carbohydrate a day which is a little higher than what most people use. Again, my physical activity is pretty darn high. But I rarely see my ketone levels, beta-hydroxybutyrate north of say like 0.4.

I had a base case of food poisoning and didn't eat for two days and I got up to 0.6. What are your thoughts around that? I'm sometimes concerned that in the process of chasing ketone levels, folks are maybe dropping protein too much, folks are just adding excess calories in the form of fat. What are your thoughts around that very thorny topic?

Sarah: Yeah. I think that's a great question. And so I have a number of thoughts on it.

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Really, especially with someone with type II diabetes, the advantages to ketones are being able to personalize and counsel that diet for sure. So, we can use the ketones to just help understand their tolerance of certain foods. So, it can be incredibly useful that way. But we still don't completely understand ketones and how essential they are to reversing type II diabetes but we have a lot of reasons to think that getting up to some level elevation of beta-hydroxybutyrate is likely advantageous.

We had the two longevity studies that came out in Cell. Another interesting way to look at this too is the diabetes world got very excited a little over a year ago when the first SGLT2 inhibitor mortality data came out. SGLT2 inhibitors are type of diabetes medication. One of the things with diabetes medications historically is that, yeah, they can acutely lower blood glucose but they don't seem to have

any improvement on cardiovascular outcomes until this class of medication came out.

There was improved cardiovascular outcome that everyone went why. Why is that? There were lots of early ideas and theories but interestingly two groups came up with the same hypothesis working totally separately in two different countries. And the hypothesis was that the cardiovascular benefit was due to elevated beta-hydroxybutyrate.

What we saw interestingly may help guide us somewhat as to the importance of this in the future. We know that the failing heart prefers beta-hydroxybutyrate as a fuel source. These patients had a slightly elevated beta-hydroxybutyrate level close to 0.3. Not what we would typically think of as all that high but it led to a significant improvement in cardiovascular outcomes.

One of the things that we have to figure out that is still an unanswered question is what you're asking. How important is it in diabetes reversal or other conditions? And is the decreased inflammation that are associated with beta-hydroxybutyrate elevation, is that part of it? Is that necessary? Is that key? What level of beta-hydroxybutyrate do we need to get to to see some of these benefits?

Maybe it's not as high as some people. Maybe it can be a slightly lower level. I think this is an unanswered question. And for our patients too. If they've reversed their type II diabetes and they're feeling good, we may increase them and they may not choose to be in nutritional ketosis long term. I will tell you most patients, because they feel so good in nutritional ketosis, that remains their goal, and they just continue to tweak and work with it. But again, that's an individualized thing. Early on, while we're teaching them, it' an incredibly useful tool for personalization.

Robb: Absolutely. I mean, that binary yes, no, in, out, that's a pretty coachable point. It's very powerful.

Sarah: It really is. I wanted to come back. I forgot to tie in the beta-hydroxybutyrate to our research results as well. One of the other really important points to the study results that came out is plaguing all nutrition trials. I actually think this is at the heart of why nutrition is such an incredibly contentious area because at the heart of all nutrition trials is a huge weakness in that the question did people actually do what you told them, is really up in the air because all we rely on is these food records.

What do we all know? I mean, what is not disputed in the nutrition world is that they stink as a measure of adherence, right? They're terrible. 24-hour food

recalls, they're just not reliable. And so, for the first time in a nutrition trial, we can say with full confidence we know our patients were doing it because their beta-hydroxybutyrate levels were elevated. What does that translate to? They were restricting carbohydrates and eating more fat and we're certain of it.

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And so that actually is one of the other things that really sets our trial apart. We didn't have to rely on those food records and dietary recalls. We were able to really use an absolute biomarker to prove that they were adhering.

Robb: It's genius. It's something that is so impressive to me about what you all are doing at Virta and it's something that for our clinic we started off in a very lipidology-centric testing kind of mode which over the course of time I've become a bit disenfranchised with relative to doing something very, very simple and binary which is looking specifically at these ketone levels and kind of having a yes-no kind of proposition which I really appreciate.

Doc, all that stuff said though, have you -- Could we make an argument that if we get beta-hydroxybutyrate levels to an appropriate spot for the individual if protein is at a level that both provide satiety but also the maintenance for muscle and immune function and whatnot, instead of chasing a specific ketone level though, we need to get some clearly and maybe it's 0.3, maybe it's 0.4, maybe it varies upon the person, but if the then peripheral trends of like downward body composition is improving, we're losing body fat, A1Cs are improving, are there some other proxies that we could bring in at that point to kind of triangulate in?

If you had someone like me where I literally am not sure what I could do to get my beta-hydroxybutyrate levels up to 1.5. I've tested it while doing Brazilian jiu-jitsu, while doing low intensity cardio. If I supplement with some MCT oil it might bump it a bit but not massively. I suspect maybe I'm just really, really fat adapted and so I'm using fatty acids as direct fuel source so I have maybe a less need specifically for ketone bodies.

But I've just seen some folks kind of run aground where they don't see ketone levels at a certain point so they add additional fat and additional fat and then their weight starts trending upwards. They actually take the most satiating diet on the planet and managed to overeat on it. I mean, are there some ways that we can intervene on that so that we can get even more customizations, still using that ketone level as a benchmark but kind of triangulate from different areas?

Sarah: I totally agree with you. The thing is, we don't understand completely. Why is your ketone level now, is lower now? Is it got to do, just as you said, with you being fat-adapted for so long? And how come that doesn't happen in everybody but it happens in some people? Why do most people's ketones -- Another interesting point is most people's ketones will rise when they exercise. But I am an exception to that. Mine actually drops.

Robb: Interesting.

Sarah: And you find those people who actually do drop. So, there's so much that we still have to learn. I think that I would say the people use ketones as a guide to make dietary changes especially early on but don't allow them to be your only measure of success because, otherwise, you get into exactly, and I've seen that before, exactly what you're saying where you can do too much of a good thing.

My favorite phrase is fat is not a free food. We want people to get comfortable eating fat and feel that they can do it but if you're consuming fat just to chase a number then you're doing yourself a disservice. This is, again, one of those things that I think it just brings to light the importance of that support and the counseling and the guidance so that people don't fall into a trap like that. Because we still got a lot to learn about it, like I said. And it can be a very effective tool but only when used properly, if you will.

Robb: Absolutely. And I love that. Again, I think the confounder for so many folks, like ten years ago I was so much more convinced about so many things then over the course of time this nuanced story has emerged in all this stuff, entering in the gut microbiome and epigenetic multigenerational signaling.

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I mean, it becomes a calculus problem pretty quickly but it's a really cool thing. Again, maybe to paraphrase or my understanding of this, is that we're using this kind of ketogenic approach that Drs. Phinney and Volek have really championed for quite a long time now where we've got an adequate protein level, we were strict carbohydrates, we use fat as a lever.

Because, clearly, when Sami did his trans-Pacific crossing in a row boat he was eating a lot of calories. But somebody who really needs to offload stored energy out of their body, we probably want all my old caloric deficit with that. Adequate protein and then adequate ketone levels are really powerful in affecting that process, but it's got to be a different story from person to person.

To your point, it's kind of nice to hear that somebody else sees our ketone levels drop while exercising. It's funny, my blood sugar doesn't really go up. I don't

really know what I'm running off of but my total energy load circulating seems to like drop. I'm not entirely sure where it's going but if we overly use a template then we don't have that ability to have the dexterity of personalized nutrition. I think that's what's so powerful about what you folks are doing.

You have this very simple story to tell up front and then as people make progress through this then we can say, okay, we're going to tweak yours a little this way and tweak yours a little bit that way and then we're able to really move everything forward.

Sarah: Yeah, you have to really learn to use the heterogeneity of responses as an advantage instead of just -- And that comes with a lot of counseling with patients because they all want to say, "Well, how come this is happening to this person and it's not happening to me?" Again, it's helping them understand that some things human to human are similar, so many things are different.

Again, yeah, the personalization and the ability to do that and do that on, again, an almost real time basis so people can just associate what they're doing with their particular biomarkers is big. And on that, you know what I think, Robb, is going to be a game changer in this field. One of the things, speaking of personalization and game changing new ideas, is going to be the continuous glucose monitors.

I just put mine on today. I just clipped mine on today so I got one. Because I've been monitoring patients on them and I decided I needed to experience it myself. These things are great because you can just look right there and see exactly what's happening when you consume certain things. And I think that this is going to be a game changer even in the people who are currently carbohydrate restricting.

People are going to quickly understand, "Hey, wait a minute, my dietician or my physician told me to eat this and look at what happens to my blood sugar? This cannot be good." We're going to get a groundswell because people are really going to be able to in absolute real time see what certain foods do to their blood sugar. I just think it's going to be fantastic. Again, taking this moment, this watershed moment and moving it forward even more.

Robb: I totally agree. I've heard scuttlebutt that even some of the wearables like Apple watches are capable of doing a pretty good job of monitoring blood glucose level. I think that they're actually trying to reach like a medical device application level and so they've really got to vet that stuff out. I think in Europe they have some RFID tags that are basically like a temporary tattoo type thing.

There's really some beautiful non-invasive technology that is going to move all this stuff forward. To your point, again, if we get that real time confirmation that that plate of enchilada is like basically put my blood sugar to 210 or something, it's like, okay, yeah, that's a real problem. We need to start modifying that stuff. And it will give folks amazing feedback so they can make better decisions.

Sarah: Yeah, absolutely. I think overall it's very exciting and it's coming at the absolute right time.

Robb: I think we're going to win this story with this kind of low carb ancestral health approach. It may be at the eleventh hour, 59 minutes. We barely avert catastrophe. But I really think that we're going to pull this thing off. But if there would be one, two, three things that we collectively, as a movement, how could we scuttle this?

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It's kind of ours to win or lose at this point, but are there some areas where it keeps you up at night a little bit where you're like, "Man, we need to fix this or we need to improve that messaging?" How could we mess this thing up now that we are at this spot where we're almost ready to win the game?

Sarah: I mean, there's a lot of points, weak links, if you will, across the system attempting to change but I say that if people want to know what they can do I would encourage everyone please to go to the Nutrition Coalition website and sign up for the newsletter. The Nutrition Coalition is a not for profit organization set up strictly to ensure that the dietary guidelines are based on the most rigorous science, best evidence.

It was the Nutrition Coalition who was able to get legislation passed in 2015 that mandated the first, essentially the first peer review of the dietary guidelines by the National Academy of Medicine. That report came out in September, last September of 2017. I mean, really pointed out what we all know. The dietary guidelines are not successful and they're not successful because they're not based on the most rigorous review of the evidence. And there's much too much special interest involved.

The Nutrition Coalition is a very different not for profit because we are not taking any industry funding. We are funded by some grants and also funding by our members too. We again are working hard to ensure that the next iteration of the guidelines which is due in 2020 does better represent the evidence and really has a rigorous review of the current science. That's what they can do. They can go to the Nutrition Coalition website, which is nutritioncoalition.us, and sign up to receive their email and consider donating. That would be fantastic.

Robb: Amazing. Awesome. I would love to see the following. I would love to see a high carb low fat vegan based Virta alternative that gets venture cap and gets infrastructure and they go to town on this because I will kind of bet dollars to donuts, to use a high carb analogy, that that process is not going to be remotely as successful as the one that you folks are doing.

It's funny, academia necessarily moves in very slow incremental fashion because things are so complex. And this is part of the reason why I'm such a big fan of market-based interventions, like the market can really figure some stuff out in remarkably fast and efficient way. I would love to see that. I would love to see some sort of venture cap back, again to high carb low fat vegan diet. Let's compare them head to head and see which one of those entities win.

Maybe, who knows, maybe we ferret out a subsection of the population that does better on that approach. It would be nice to know. I think, again, if we were to start getting one, two, three standard deviations out, it's still going to be this low carb approach that takes the most boxes and fixes the most problems simultaneously.

Sarah: Yeah, absolutely. It would be fantastic to see. The problem again, really just the physiology, even if you really get into some of the studies on the very high carbohydrate dietary interventions, even the American Diabetes Association, this is interesting, this is an interesting little tidbit, they actually acknowledge that there's really not any evidence that the very high carbohydrate vegetarian or plant based diets improve glycemic control or cardiovascular risk factors unless they're significantly calorie restricted. I mean, the ADA actually says that in their document and then yet goes on to recommend them as an eating pattern which is semi-comical.

Robb: Ridiculous, yeah. The irony there is even if it is high in carbohydrate as a percentage of calories consumed but calorie restricted, what do we end up with? A ketogenic diet. You're going to, if you calorie restrict sufficiently, even like some of the early CRAN studies where they were like 40% calorie restricted, they still had measurable levels of beta-hydroxybutyrate.

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And how many people, when you really talk about compliance, trying to starve people over the long haul and have them in a hypoglycemic rollercoaster, that's just not going to play out that well.

Sarah: No. And let me just point out one other interesting thing about the low fat high carbohydrate vegetarian based diets, is that when you dive into the studies, one

of the other things that you see, which is really concerning, is that even in cases where maybe they get like basal insulin down, for example, what they see is that your 24-hour insulin doesn't change in many of these studies or glucose. And so what's happening is that they are inducing these really big postprandial blood sugar surges.

What we know, and it's very well documented in the literature, is that the postprandial surges significantly increase the risk for cardiovascular disease. And so, once again, another big advantage is that we know that low carb hydrating high fat diets can cause completely flat line 24-hour blood sugars. That's just yet another angle where this approach can be a benefit to someone's health.

Robb: Doc, correct me if I'm wrong but when I read those papers on the blood sugar surges related to cardiac events, you could almost make a case that absent those blood sugar surges, we're not really seeing cardiac events. I mean, is that an oversimplification of that research today?

Sarah: We're not seeing cardiovascular events in patients who are eating a vegetarian diet or -- I'm sorry?

Robb: Basically, like you could possibly make an argument -- Again, this is maybe stretching the facts a bit, but if we don't have blood sugar excursions we just don't see cardiac events.

Sarah: Well, and I think that they're certainly lower. I think that there are some other things that could be playing a role even in people who don't have the blood sugar surges, excuse me. But I think it's a major player in cardiovascular events.

Robb: Right. Well, that's me making things. That's the tendency, is to make this stuff overly simplistic amidst the nuance. So, Doc, I know you have some folks there, boots on the ground that you need to go meet with here pretty soon. So tickled and excited about the work you folks are doing. Where can the listeners track you down and track more information down about Virta?

Sarah: They can go to virtahealth.com and they can follow the blog. We've got a lot of fantastic educational pieces there, some by, again, the leaders in the field. Steve Phinney and Jeff Volek write quite a bit. And so I encourage everyone to go there, find out what we're all about. Again, we're constantly increasing and updating our educational content. So, people hopefully can get there and learn a lot as well.

Robb: Awesome. Doc, would you be game to come back on as these next rounds of studies looking at cardiovascular disease processes and then also I believe you

mentioned liver metabolism, when that data pops up in the peer-reviewed literature, do you mind coming back on and maybe unpacking that material as well?

Sarah: I'd love to. I'd love to talk about them. Yes, absolutely.

Robb: Awesome. Well, we will make that happen, and looking forward to seeing you in real life. Are you going to be out at Paleo f(x) or Low Carb USA or anything? Or are you too busy actually saving folks' lives to go to those endeavors?

Sarah: I am going to be -- My next big meeting is going to actually be in Zurich going to the BMJ and Swiss Re Conference there which I think is going to be a really exciting one, and then a number of other conferences over the summer. It's going to be a busy few months but, again, it's worth it. It's a fantastic space to be in and it's just such an honor to be helping and partnering with patients as they improve their health.

Robb: I'm glad you transitioned out of the PhD track and I'm also glad that you didn't head into a cardiology. We might have a very different picture of this whole thing had you made different decisions. Thank you for the hard work you've done and the decisions you've made. I'm really looking forward to getting you back on the show and unpacking more of this amazing story.

Sarah: Thanks so much. Remember, embrace the pivots. That's what I say. And I'm so glad you have been able to be here with you today. Thanks so much for all you do, Robb.

Robb: Thanks, Doc. We'll talk to you soon.

Sarah: All right. Take care.

[1:00:02]

Robb: Bye. Thanks again for listening to the Paleo Solution podcast. Here's a quick message from one of our sponsors.

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