

## How to Manage Sugar for a Better Brain and a Longer Life – Colleen Cutcliffe, Ph.D. – #943

Dave Asprey:

You're listening to the Human Upgrade with Dave Asprey. Today, we are going to be talking about gut metabolism and your microbiome and sugar. We're going to talk about hacking your brain and how sharp your brain is and how long you're going to live and the weird interactions between all of those things. We're going to go deep on blood glucose range and what fluctuations mean. And that's because there's been a lot of talk lately about what happens if your blood sugar spikes and then comes down really quickly. And how important is it to avoid, what's called a postprandial spike? Strategies to do that and what it can do to other parts of your biology and even different types of blood glucose tracking. End of the day, though, the goal of this episode is how do you improve your focus, your sharpness, and your mental endurance. So who would be best to talk about this?

Because we know a lot of experts who've been on the show. Well, Colleen Cutcliffe, who's a PhD and the co-founder of Pendulum Therapeutics is uniquely well suited to talk about this intersection of your gut, sugar and your brain, because she works all day long on finding new bacterial strains that change your blood sugar response. In other words, why should you make your body do it when you can have something in your gut do it for you. And she's very into longevity as well. And we're going to just figure out the relationships between sugar management, longevity and acuity. Colleen, welcome back to the show.

Colleen Cutcliffe, Ph.D.:

Thanks so much for having me.

Dave:

I love getting a chance to interview you because having the Ph.D. in molecular biology gives you a different mindset than say a functional medicine doctor or something like that, where you kind of think of it more like an engineer, which I appreciate.

And we've talked about toxins in gut lining and we've talked about type 2 diabetes interventions using bacteria instead of drugs. So we're going to go deeper though on brain health and aging. So what's new? Okay. We know [inaudible 00:02:19] from your gut. You already told us that. What about the brain? Why is this an important thing to go into?

Colleen:

Well, I think it's a really interesting new set of research that's coming out around the different pillars of healthy living. And really we know that for ourselves and we think about what does it mean to age in a healthy way? What are the things that we're all trying to hold onto as we exit youth and enter the aging process. And I think at the end of the day, there's two really big things. One is our metabolism. We all want our metabolism to stay as strong as it was when we were younger. And the other, is our mental acuity.

So as you age, you start to realize your metabolism slows down. You start to get a little bit more memory loss, cognition's a little bit slower. And so how do we maintain a high performing metabolism and brain function? And I think the interesting thing we're going to talk about today is how those two things are actually linked to each other. It's not accidental that these things start to decline simultaneously. And then what is the role of the gut microbiome in all of this? All of the things that we do to try to change our diet and our exercise to improve both our metabolism and our mental acuity are

kind of forgetting the third pillar, which is the microbiome. And we're starting to understand what role the microbiome can play in both of these really important pillars to healthy living.

Dave:

I'm constantly intrigued by research on mice, sterile mice that have no gut bacteria whatsoever. They seem to be able to eat anything and stay young and lean and ripped. So how do you know the microbiome's good for anything at all?

Colleen:

Well, despite lots of research being done on mice and lots of drug development going through lots of mice, we are actually not mice. And so I always laugh that if you're a mouse and you get cancer, you're made, there are hundreds of thousands of drugs that can help you. And very few of those actually work in humans. And I think that there's a jump between mice and humans, just from a genetic and systems standpoint. But it's even deeper when you talk about the microbiome, just think about the diet of a mouse versus the diet of a person, versus the diet of a person on a Western diet and the way that the microbiome interacts with your system. I'm not saying you can't learn anything from mouse studies, but I'm saying we have to be really careful about trying to directly translate what we see in mice to what we see in humans.

And so there are some things that have translated. For example, we know that when humans get gastric bypass surgery, they can have these immediate changes in their metabolism. And you could see that also happening in mice. And we know that if you do these fecal transplants in mice, that you can change their metabolism, you can make them obese or skinny. And we see that also in humans. And so there are some things that are translating around the microbiome, but where it starts to get more complicated is when we start to get more targeted than just I'm going to remove your entire microbiome, or I'm going to whole hog supplement it with an entirely different microbiome. So getting specific and into these very targeted pathways, now becomes a little harder to translate.

Dave:

If we took a human and we removed all of their gut bacteria, what would happen?

Colleen:

Well, that's essentially somebody who's gotten gastric bypass surgery. And I think, what we know is that, you start to have extreme food sensitivities. So your microbiome is really there to help you metabolize your foods. And first place, all your food goes is through your stomach and into your GI tract. And so I think we don't fully understand the implications of this full surgery or you move the entire system. And I haven't really delved into that, but I think it would be dramatic if all of a sudden today you had no microbiome. You would know.

Dave:

You would know, but you might also improve if you had a bad microbiome. And the reality though is unless you're going to be Bubble Boy from that movie in the 70s or whatever, where you never get access to any bacteria and all of your food is sterilized and given to you through an airlock, it's not really reasonable. But I'm always interested in these edge cases that can be really instructive. And I still, it kind of makes you mad that a mouse can have no bacteria and completely kick ass, but then as soon as you give them bacteria, they get really fat, if they get normal gut thing. So we know that they're major players. There's been so much that you've talked about and others on the show about microbiome's

important, it's an essential thing there. But there's been only a little bit of talk about subtle fluctuations in blood glucose.

So over the past 20 years, you could do what I did when the doctor said, maybe you have high blood sugar when nothing works. So I pricked my finger a whole bunch and drew a graph and I'm like, I don't think I have very high blood sugar. It wasn't terrible. And although my fasting was like 118, I think it's now something like 85, 83. But that wasn't, 140, 150 and much higher, but it was prediabetic. So not unhealthy, but not the cause of all my problems. Now, since then meters have gotten cheaper and faster and better, and we have continuous glucose monitoring, which has had a lot of people start paying attention to their daily fluctuations you would've never seen before. And you get the slope of the curve. How important is that? You have hundreds of thousands of people drawing these curves going, oh my God, I ate two grapes and look what it did. I'm going to die. What's your take on CGM?

Colleen:

Well, I'm a scientist, so I'm always going to say more data is better. And I think that when you're trying to make improvements and you're making these micro adjustments in your life and you want to understand what impact are they having? A continuous glucose monitor is a great way to understand for your body, how does your glucose respond to different meals, and different foods that you're putting into your body and trying to understand how you can change that I think is really important.

For example, I wore a CGM and saw the difference that my body had when I drank a glass of orange juice versus a glass of grapefruit juice. In reality, I can't feel any of that difference, but when you look at a CGM, you can start to understand, is one better for me than another? And I think what we've started to realize is, it's not just for people that have type 2 diabetes, that's important to understand your glucose responses, but for all of us who are... Again, this is about aging, about having increased glucose spikes and more extreme glucose crashes as you age that's part of the process.

And so the things that we can do to try to improve those are things that we wouldn't know unless we are actually measuring them. So I am a big fan of CGMs and data is great.

Dave:

What I'm really excited about is that when we get enough data from enough people, whether it's sleep data, EEG data, continuous glucose data, over longer periods of time, the continuous monitoring, we're going to find all sorts of cool stuff about the human condition that no one ever knew, and that you could never get in a university lab because the sample size isn't big enough. And I feel like we're getting to that point with CGM data, where there's just enough people doing stuff and maybe the actual window in your blood sugar should return to normal, right now it's about two hours, right?

You eat something with carbs, two hours later, your blood sugar should be back to mostly normal. How do you look at that time? What does mostly normal mean? What should it look like based on what we think now, but we may find out two years now that it should be actually, two hours and six minutes is really important. And we just don't know because we used to have about two hours in 1970 and we still stick with it. What's your take on what it should look like if you eat a normal amount of carbs?

Colleen:

Yeah. I think there's the time component, but then there's also the peak component. So when you think about, you have sugar, it's really a curve of the sugar getting into your bloodstream that goes up and then down. And so it's really the area under that curve that I think is more relevant than even just the

time. Because if you can reduce the level of that spike, but the time stays the same, the area will go down and that's better. What we're going to talk about today, I think is, what are some of the other things that happen when you could manage your sugar and those postprandial glucose spikes better? And for Pendulum, we really worked hard on how do you modulate those post postprandial glucose spikes through the microbiome.

And we created a product that allows you to lower those blood glucose spikes, 33 to 34% for people with type 2 diabetes. And I think we all knew that was great. And that was going to be wonderful for people with type 2 diabetes. What we didn't realize was how many people who don't have type two diabetes were going to end up buying the product and benefiting from it. So less than half of our customers actually have diabetes.

And so who are these other people that are taking? And what are the benefits that they're reaping? It's not just this lowered blood sugar spikes, but it's really all of these other, so-called soft benefits that in science, we don't fully understand, including reduced brain fog, increased sharpness, increased focus. All of these things that are linked to having this reduced blood sugar spike people are experiencing that and we're now starting to understand that those two things are actually tied to each other.

Dave:

So you don't worry too much about how long it takes to return to normal. You worry more about how high the spike goes?

Colleen:

I worry about the area under the curve.

Dave:

Okay. So neither access is more important. If I only go up to 110, but it's for four hours, that's just as bad as going up to 130 for two hours. Let's say. If the area under the curve is the same?

Colleen:

If the area under the curve is the same. Yeah. I think that's the primary output that's read out from CGM. And this is really born from the old school, oral glucose tolerance tests or meal tolerance tests, where it's the area under the curve that appears to be the important metric.

Dave:

Got it. So you don't want to spike quickly, but okay. Let's say, we have someone who drinks orange juice and they spiked at 220, but they're back to normal in 15 minutes. You're not worried?

Colleen:

Well, what's the area under that curve?

Dave:

Well, what I'm saying. If it was the same as, okay, they only went from 85 to 100, but if it's the same under the curve, you just don't care if it takes 10 hours to recover? And a lot of people are asking me, this, they're saying Dave, I tried a different glucose monitor and there was a 10 second wiggle. I don't think we know that much, but I kind of with my own thing, as long as I recover in two hours.

And this spike isn't very high, I don't really worry about it. Right? Especially if I had a whole bunch of white rice or something, and I didn't spike a lot. It's like not that big of a deal, but if it took me three hours and it was a lower spike, I'd probably be going, huh? My time to return to normal doesn't seem right. But maybe I'm thinking about it wrong because you're saying area under the curve is all that matters.

Colleen:

Well, first of all, I agree with you. We're very early in this research and from individual to individual, it's different, but you might consider, and I'm not saying that this is the truth, but you might consider that the goal in life is not to be going like this, but to actually be moderating more like this. And that really gets to the area under the curve. And so you might say, well, if we're just trying to keep the body from getting into these spikes and crashes, you might accept a longer time to metabolize if it was not as high of a spike.

Dave:

Okay. So you like a lower spike more than time to resolution. So you would actually favor a longer resolution versus a short spike, as long as the same area under the curve. Okay. This is important data for anyone who's looking at their blood sugar, because some people lose their mind. Like, oh my God, you know, it took me a long period of time to come back to normal, but I didn't spike high.

And so you're saying those people are probably okay, but the people who eat something and just go through the roof and come back down, they're the ones who worry about the most. When you modulate gut bacteria using like the Akkermansia species in Pendulum, what do you see? Does change? So the spikes aren't as high or does it make it so people resolve and come back to normal more quickly?

Colleen:

It does both, but in people with diabetes where you had this really exacerbated postprandial response, it really pulls down, for a lot of people, it's that really high peak. It really pulls it down. But again, it's really an area under the curve measurement. And honestly, the two hour timeframe that's been historically used, it's not so far off. For most people, it is somewhere in the 120 minutes that you come back to normal. It's quite rare that people go out to four hours or metabolize it all in 30 minutes when it comes to meals.

Dave:

Is there such a thing as good sugar?

Colleen:

If you asked me? I think all sugar is good sugar.

Dave:

Okay. Fair point. Yeah. I guess your middle name, if mine is danger now apparently yours is give me some candy. That'll be... So yes, all sugar tastes good, but people talk about good sugar and bad sugar, and good protein and bad protein, are some sugars tolerable in your world?

Colleen:

I'm being serious when I say that. Sugars are tolerable. Especially, we know, don't eat the fake sugars, try to get sugars through foods as opposed to processed and things like that.

Dave:

You're okay with sucrose then? Just straight up table sugar?

Colleen:

I am okay with table sugar because I know that on my product, it helps me metabolize it.

Dave:

Okay. So you're saying if your gut can handle it, you have some sugar. And your blood sugar goes up briefly and not too high and then comes back down to normal. What's the harm in sugar?

Colleen:

I think that our bodies have evolved to be able to metabolize sugars. And so cane sugars and table sugar and things like that are different than artificial sweeteners.

Dave:

No, those are bad.

Colleen:

Right. So our body is able to metabolize things like cane sugar and certainly sugars from fruits and things like that. It's just that we live in an age now where we have unlimited supply of those things. And so how do we now help the rest of our body figure out how to metabolize those foods better? Of course, I'm going to tell you the right thing is you should never have an overabundance of sugar and you should try to... Moderation in all things is good and things like that.

Dave:

And by the way, I share your opinion. Unless you're actively pursuing a keto phase of the Bulletproof Diet or something, you should be able to handle a teaspoon or two of sugar, whether it's in a piece of fruit, or whether you sprinkled it on your pork chop to make it taste better. Right. And if your blood sugar doesn't spike quantitatively, when you do that, probably means your gut bacteria, or maybe you did some squats or something. But all right, good. You should be able to handle it, right?

Colleen:

You should be able to handle it. And I'll tell you something too, in the foods that we consume. It's not just about the sugars that we eat, but it's the other foods that we eat too, that can help us also modulate that sugar. So for example, we talked a little bit about this last time, but the consumption of polyphenols can feed specific bacteria in your gut. And so we know polyphenols are linked to higher Akkermansia levels and the formulation that we have, we know that Akkermansia is a big participant in helping metabolize sugars.

So if you're consuming, foods and beverages that help get you the right microbiome alongside these sugars, you're basically giving your body both the sugar and the tool to metabolize that sugar. And I don't want to get too much into your territory, but you probably know quite well that one of the big

sources of polyphenols is coffee. And so it's interesting to think about what coffee is doing for your microbiome to actually help you also metabolize these sugars.

Dave:

Okay. Let me ask you this then. Can I put a teaspoon of sugar in my coffee?

Colleen:

I should ask you that. You're the guru when it comes to how to take your coffee in the most optimal way. You don't think there's sugar in your coffee, right?

Dave:

Well, if you're metabolically healthy, you're not intermittent fasting and it makes you abundantly happy. It's not causing a big blood sugar spike, and you don't have candida and it's not going to throw your gut bacteria off, which it probably won't, if they're healthy. I don't see a problem with it.

However, most people, when they do that, it doesn't do that to them because their metabolism isn't there. And also look, if you're going to be exercising much, it probably doesn't matter, if you're going to go for a walk after that. We're talking about a teaspoon. You want to put four tablespoons in your coffee. I think that's just always bad for you. I don't care what gut bacteria you have. Do you agree with me though or?

Colleen:

I do agree with you. I don't even know why you have the coffee, you should just have the sugar.

Dave:

Well, isn't that what you do when you go to your favorite green logo, coffee shop these days.

Colleen:

That is what sells.

Dave:

I'm having a rainbow unicorn captain crunch fruity pebbles latte right now. Now do you imagine a science fiction based future where I could take the magic Pendulum or other combination of probiotics and just be like, I can be a sugar monster. I'm going to just chow down on the donuts.

I'm going to have all these engineered gut bacteria. They're going to eat all the sugar for me and turn it into butyric acid. And it's going to take all the bad fats and turn them into long chain fats. And like I'm going to be a garbage eater and just so thin and ripped and happy and young and all that. Do you think that might be possible?

Colleen:

Well, if we're talking science fiction, I think anything's possible. When we're talking about reality, unlikely. Mostly because when you think about it, there's just sort of a physical constraint. So you've got a GI tract, that's a certain size. And so if everything that you consume is a higher input, then you can metabolize that you won't be able to catch up to that.

What we can imagine though, is a world in which you don't have to be on entire sugar lockdown, and you are able to help your body metabolize those sugars better, or that as you age and you lose the ability to metabolize these sugars, you can start to give yourself back some of those tools so that you can metabolize better.

Dave:

If someone stops eating sugar, are they going to live longer?

Colleen:

Well, you can't completely cut out sugar. You do need sugar. Let's remember that not all sugar is bad for you all the time. So first of all, every cell in your body, except for your colon cells need glucose in order to survive, in order to replicate, in order to perform functions. So all of the things that allow you to be a human being require some amount of sugar.

Dave:

But gluconeogenesis... Sorry. I'm sounding like one of the dirty keto apologist. If you eat another carbs again, you're bad. Doesn't the body just make enough sugar for that stuff? So you should just never eat it.

Colleen:

Well, the answer is you have to consume some amount of sugar, but maybe the question is, can you get enough of that just through the foods that you're eating and you don't need the teaspoon of sugar in your coffee or the donut or the dessert? And that's a fair point. We haven't evolved to have to consume large amounts of sugar.

Dave:

Okay. So if I cut out all sugar, but what I find in my relatively low carb, but not sugar free diet, and I don't need any added sugar. Is it going to make me live longer? Do you think? We have some studies, but this is an opinion. And asking PhDs to give their opinion is like pulling teeth without anesthetic, but I know you're going to do it.

Colleen:

You may not live longer, but it'll feel longer.

Dave:

Ooh, I like that answer. So it turns out there's value in pleasure, right? So maybe sometimes eating some sugar, but maybe not fried with canola oil and [inaudible 00:23:15], is a good strategy for longevity. Right? And I actually agree with you and it's funny, sugar reduces stress response. Sugar helps people when a migraine is coming on. Even orange juice, surprisingly radically reduces lip polysaccharide formation when you're having really bad food poisoning, because it shifts some stuff with your gut microbiome.

There's that idea like if sugar bad, no sugar good. And I think it's more nuanced than that. And some occasional use of ideally natural sugars and that are present with some other stuff. It's probably not going to kill you and avoiding it religiously and scrupulously may not be beneficial, but for most

people, if you start with a teaspoon of coffee every morning, next month, it'll be two teaspoons. The next month it'll be three teaspoons, because it's habit forming and addictive, right?

Colleen:

Sugar and caffeine are addictive. When you put them together, that's definitely an addiction. Yes.

Dave:

It's so good though. So all right. If I have bacteria in my gut say Pendulum that you've got the data showing it reduces the blood sugar spike. Does it make sugar less addictive? Do you think? You could have a study on sugar addiction and Akkermansia, but does lower spikes in blood sugar equal less addiction?

Colleen:

It's pretty interesting. One of the unexpected things that we've learned from our customers is that it can reduce sugar cravings. And so we have people who are on the product religiously because for them it reduces their cravings of sweets. And I don't know if that's as much from necessarily that your body's metabolizing sugar's better and that's what leads to the reduced sugar cravings.

But there is this gut brain connection. And we do know that the gut generates neurotransmitters that make their way to the brain, dopamine, serotonin all of these different things. And so I think we don't understand where we get these cravings from and what can mitigate them, but it does appear that there's something in the microbiome that can help you alter your cravings.

Dave:

What I deduced and read some papers on, early on when I was getting off of sugar, when I was losing my 100 pounds. And by the way, I'm not all the way off sugar, I'll eat 72 or 80% chocolate that has sugar for the rest of it. And I just don't care. My body handles it just fine. In fact, I sometimes don't even see a blood sugar swing at all on the monitor. And sometimes it's like five or 10 points. I don't care. I like my chocolate. It's good for me. And I'll spend my sugar points there versus some sort of weird other thing that someone thinks is healthy, like grape nuts or whatever. So when we look at getting off of sugar though, I learned, okay, if your bacteria and your gut are used to eating sugar, they rely on it.

And you've actually modulated the population to expect quick sugars. And if you eat a lot of sugar, your gut bacteria shifts. And then when they don't get the sugar they were expecting, they start getting stressed. And when they get stressed, they exhibit bacterial fight or flight response, which is well we're bacteria. We can't really run away. Let's just put out some lipopolysaccharides, which are our defense molecules when we're stressed. Which happen to be things that cause brain fog, aging, systemic inflammation, and sorts of other bad stuff.

So you feel worse and worse as your LPS levels go up until you feed the little terrorists and then they calm down and then they stop giving you food cravings for a little while longer. So some of it is from your blood sugar rising and then getting hypoglycemia and crashing. But some of it is based on lipopolysaccharides coming from bad bacteria that you have, because you ate too much sugar. Now, that's me putting the story together from a bunch of information and just from what I could tell by binding lipopolysaccharides. Take charcoal, sugar craving goes away. That's interesting. Poke holes in my theory. Tell me where it's right. Tell me where it's wrong.

Colleen:

Well, I think the theory is all of it makes sense to the one point, which is that you have to feed the little terrorists. So here's where there is an opportunity for you to take charge here, which is to say that they still require you to feed them in order to live. And bacteria in your gut can die and they can be... It's an ecosystem so they can be replaced with other bacteria that are more beneficial for you. And so while there may be a temporary gross feeling and increased brain fog and all of this stuff, if you push through that...

And a lot of people who do extreme diets and things like that, experiences this. Where in the very beginning... Of maybe any diet, doesn't have to be extreme, but any diet, in the beginning, sometimes you actually feel worse. But then when you push through that, you feel much better on the other side of it. And so the same thing here is if you don't feed those sugars and you don't give those bacteria back their food and you push through that and then you start eating more fibers and now you're constituting your microbiome with more fiber metabolizing, more short chain fatty acid producing strains, and come on the other side of that, you're going to have a much healthier and you're going to feel a healthier microbiome.

Dave:

A lot of people talk about getting a keto flu. So I tried ketosis for the first time and I feel like I was going to die for three days. And then I felt amazing. Yeah, that's kind of bacterial die off, a lot of it and maybe some hypoglycemia, but just take some charcoal during that. And magically you don't have keto flu, like who would've ever thought. So I'm pretty sure that's a gut toxin response. Do you buy that? Or is there another thing happening when people just go cold turkey off carbs except for fiber?

Colleen:

Well, I'm a microbiome all day, all night, 24/7. So of course I think, it is your microbiome. The first place all your food goes to be metabolized is your microbiome. And you're trying to whole hog change this, the food that you're giving it. And so I do believe that, that's where it is all centered.

Dave:

Okay. So when people talk about healthy metabolism, generally, there's three buckets, maybe four. There's diet, there's exercise, there's microbiome and the fourth one might be breathing, because that's the other side of eating. If you don't have air and you don't get it in, right, you don't combine it with the food, your metabolism is also broken.

But let's take breathing out. So you have diet exercise and microbiome. Allocate a percentage of importance to each one of those, for someone to have a healthy metabolism. I love asking questions that you don't have studies on, but you know this intuitively, so give me your best guess.

Colleen:

Well, I'm going to take your three pillars. I'm going to turn them into two. So your diet is inextricably linked to your microbiome. So I'm going to say that when you change your diet, you're actually changing your microbiome and that's what's helping with your metabolism. And so between your microbiome/food and exercise, I think it's 75% the food and microbiome, and 25% your exercise. Obviously, based on exactly no studies.

Dave:

There probably are some studies in there. There have to be. But I think you're actually quite low. I think it's like 90, 10, maybe 80...

Colleen:

Yeah. Maybe it's 90, 10. Yeah. Maybe I would agree with that. I would go higher. You're right.

Dave:

You can take someone who barely does anything and you just change their diet and like, oh my God, I grew abs. Isn't that interesting? Not that exercise, isn't good for you. It is. But in terms of changing your metabolism. Yeah, having more muscle mass, right? That's a good thing because it's going to burn more calories and having more brown fat from cold exposure or fasting or whatever.

Sure. Those are all good. But in terms of moving the needle, you can do all the exercise in the world you want and live on potato chips and you're still going to be fat. Right? At least some people will be, maybe not everyone. And the people like me who stay fat, no matter how much I exercised. And I really pushed, it was all microbiome and other metabolic dysfunction. Okay. So you're a 75, 25 or maybe higher person.

Colleen:

I might add in, maybe the reason I give a little bit more to the exercise part is that I'm also baking and I think that for many people and this is true for me, that exercise changes my mental state. So if I don't exercise, I get kind of down. But it's a cycle. So that can contribute to poor eating habits and worse metabolism, [inaudible 00:32:03] mental state.

Dave:

It sounds, you have an addiction problem.

Colleen:

I have multiple addiction problems.

Dave:

I have a friend who said exactly the same thing, but it was about heroin. And it's so weird. I guess they're both affecting your opioid system. So okay. I respect your addiction and we're all here to support you. That said, yes. Exercise helps with your mindset and your mental state, and blood flow to the brain.

All right. Here's a tough one for you. Okay. Someone's standing in front of you and in one hand... Again, they're going to eat a bowl of ice cream. Okay. And in one hand they have Pendulum, the probiotic that helps with blood sugar control. On the other hand, they have instructions to do 40 deep air squats after they eat, which one's going to have the best blood sugar response after eating the ice cream?

Colleen:

They haven't been on Pendulum Glucose Control?

Dave:

Okay. Let's assume one person's taking Pendulum regularly, the other isn't and there's a choice between air squats versus being on Pendulum. Who's going to respond better?

Colleen:

Oh, Pendulum for sure. A bunch of air squats [inaudible 00:33:13] that's too temporal. Yeah. You're having the good microbiome. That's the key.

Dave:

Okay. I think you're right on that. That's been my experience. And when you do have the sugar, having fat with the sugar, which is going to off half the keto community, that actually does control blood sugar pretty nicely.

And having protein also controls it pretty nicely. And certainly the fiber, we know, slows it down and changes how it's fermented. Another name for fiber is prebiotics. Right? And you put a few prebiotics in Pendulum, right? Isn't there some sort of growth substrate in it?

Colleen:

Yes, we inulin in there, but we actually have it in the pill because the idea is that, when the strains are ready to be revived and come to life, you want to have the food right there next to them. And we actually found... I know I was just slamming on mouse studies, but we did find in these animal studies that if you didn't have the prebiotic with the strains, you didn't get the same level of efficacy as if you had it there. So really they function together.

Dave:

Okay. I think you've got a point there. They do function together.

Colleen:

Well, the overall optimization of your health requires you to believe that all these systems are actually talking to each other. And so going extreme on one thing at the expense of another thing is really not great. And so when I talk about like donuts and... And I hate exercising, but I know that if I don't do it, I don't feel very good mentally.

And so all of these things are related. So the idea of having, once a week indulgence or allowing yourself to do things that feel really good to you is important because actually your mental state of mind is linked to your metabolism, and your health, and your immune response, and your inflammatory response. So all these things are linked. So really, unless it feels good to be a saint that isn't doing anything sinful, you got to have a little sin in your life. It's good for you.

Dave:

Do you think that having a healthy gut biome as even a very young child is likely to contribute to long life? Do we have any data about that?

Colleen:

There is a lot of data showing that the infant gut microbiome, and the toddler gut microbiome, and the youth microbiome is super important in particular, how your immune inflammatory responses develop.

And so this is a really fascinating part of microbiome science, which is to say that, infants that are C-section versus vaginally born, infants that are on breast milk versus formula, what foods they start eating initially, there's a lot of work around a very particular strain, the bifidobacterium infantis, that is very high in infants, and that if it's low it's problematic.

So I think the early gut microbiome of a human we know shapes the immune response. And if you believe that the immune response is important for healthy aging, which I do. And I think many people do, it's important how you start.

Dave:

For both of my kids when they were just starting to nurse, within 48 hours of birth, we opened capsules of the infantis strain bacteria and put them on Lana's nipples so that the kids would get extra of those bacterial strains, because there's so much good evidence for it.

Because kids microbiome shifts really dramatically in the first year and as they start eating food and all, do we know what age we start having more Akkermansia? Which is one of the main actives in Pendulum. I know you have several, but.

Colleen:

Yeah, I don't know at what age Akkermansia really starts to appear as a key strain. Certainly, there's a lot of studies in adolescence showing that when you put them onto a better higher fiber diet, they get increased Akkermansia, that's all associated with better metabolism and weight loss. But I actually don't know the earliest age at which you start to see that really take a foothold. It's a great question.

Dave:

One of the problems is that, we just don't have good data on this. You need a large sample size, right? And you need frequent poops and who wants to take frequent poop samples every day from a baby up to age five? I don't think that study's ever been done even on weekly, much less daily basis.

But that's the kind of granularity of data you probably could get, if you have 5 million people's poop samples at different ages. Which is really interesting, that's where biohacking and big data and all the cool stuff we could do. Now, we're going to know it, whether we run a study or not, we just don't know it yet. Right.

Colleen:

Absolutely. And honestly, if there were a way to enable people to get that data. When you have a newborn or you have an infant you're in their poop multiple times a day, it wouldn't be very hard to actually sample every day, multiple times a day, at least for that first, whatever, two years, three years of life.

So if there were a way to actually take a swab and get readouts of these different strains, that would be amazing. Yeah. We just don't have the data.

Dave:

One of the things that I came across when I was doing all the research for my anti-aging book for superhuman. It was about how you can predict someone's age just by looking at their poop and looking at the ratio of sugar consuming bacteria and the diversity of bacteria.

So a marker for being younger is more diverse and more able to handle sugar gut bacteria. Why do we get that as we age? Why does our gut bacteria population shrink? What do you know about that? And what do you know about using Pendulum or Akkermansia in order to fix it?

Colleen:

Yeah. This is one of the things about the gut microbiome that is really interesting because, we know that diet and antibiotics and all these different things can shape the gut microbiome. And those are things that are under our control, we consume. But there are a lot of things that shape the microbiome, deplete the microbiome that we don't have control over and aging is one of them. Stress is another one.

We know that when you're undergoing more stress, you actually have a less diverse microbiome, even though you're not really changing anything in your diet. Same thing with circadian rhythm. Actually, if you travel a lot and you go to different time zones, that also depletes your microbiome. For women, when you go through menopause, that also depletes the microbiome. So there are all these different things that deplete the microbiome that are just actually part of life, stress, aging, travel. And so alcohol. But alcohol, you have control over presumably. But the idea is that there are all these things that are outside of your control, that are causing your microbiome to become depleted and really the key...

And this was for me, very fascinating because the key is to understand, what are the specific things that are getting depleted, that are causing you to lose these functions, that show up in your health? And that's really, I think the core of it. And even we go back and talk about kids. I started this company actually because my older daughter was born prematurely and was given multiple doses of antibiotics. And multiple studies have shown that children and infants who are systematically in antibiotics are systematically more prone to chronic illnesses later on in life like diabetes, like ADHD, like celiac disease.

And so I noticed that my daughter was having food sensitivities as she entered elementary school, sort of put two and two together and realized, okay, this early start of life where she had a depleted microbiome is causing her to be susceptible to these chronic illnesses. What are the key things that we can give her back? And I think as we age, that's what we're trying to figure out.

Dave:

It's really interesting that studies show at least in animals, that if you improve your glucose control, neurological inflammation goes down and cognition goes up. And I think even some of the many different contributors to autism is probably based on the microbiome. In fact, that's almost certainly based on the microbiome and glucose control.

I'm not saying that's the only thing. And I don't think there's any one cause for autism, which is basically autoimmune neurological inflammation from multiple causes along with mitochondrial function. So like, gee, I wonder if the gut bacteria population is a player, of course it is, but the fact that you can improve glucose control and then in those studies improve cognition, mouse cognition is like solving mazes and stuff. Do we know how much you have to improve glucose control to change inflammation markers or improve cognition?

Colleen:

Well, those are animal studies and they're relatively recent. And so I think trying to understand that link is pretty new. But it's interesting. We do have customers who are on the product for traditional neuronal diseases. So things like seizures, and autism and, things like that. And you probably know quite

well how those things are linked to diet and therefore the microbiome. But this idea, it's been known for a long time that if you have reduced glucose control, it results in these poor mental acuity. So like lower memory, lower cognition, there's even these studies where they've done these sorts of executive tests on people where they give you a variety of resources and your ability to take those resources to achieve a goal is actually diminished when you've got uncontrolled blood glucose.

And so I think that, we know that lower cognition is linked to poor glucose control. And what people are starting to understand now is, all right, but if I have better glucose control, then do I get better memory cognition, mental acuity. And you probably know that a lot of people are trying to manage their blood glucose through a variety of different methods, pharmaceuticals, foods, and things like that. And I think this is sort of the surprising result, is that people are realizing they're having improved focus, improved sharpness, improved mental acuity when they're able to manage their sugars.

Dave:

And you did surveys of people who take Pendulum and you found that they're saying they felt more energy, more mental sharpness, but are they doing the glucose control or the Akkermansia product? Because you have both as separate products. Does one work better for mental sharpness than the other?

Colleen:

That data that we've done is really coming from the glucose control customers.

Dave:

Just glucose control. Okay.

Colleen:

Yeah. I don't know that we have enough data points from the Akkermansia customers to feel like we're seeing trending there. And I think that with the glucose control customers after they've been on it for a while and they've really gotten their glucose stabilized, they start to experience these things. But yeah, it's really the glucose control product where we're seeing this.

Dave:

Okay. One of the other questions that I was about to ask you, that also one of the upgraded collective audience just typed in. Is, let's say someone has some problems with blood sugar control, at least after meals. Metformin. Should they take Metformin and Pendulum? Do they interact? What does Metformin do to your gut bacteria?

Colleen:

Well, there are quite a few studies showing that Metformin impacts your gut microbiome. Unfortunately, a lot of them are counter to each other. So some of them say like, well, they increase these types of strains, the other one say, well, they decrease those exact types of strains.

And so I think it's not clear actually how Metformin impacts the microbiome, but I will say this, that we have a lot of... Actually we have clinical trial data, but also real life customer data of people who are on Metformin and seeing the effect of Pendulum glucose control is on top of Metformin. So the two appear to have an additive effect.

Dave:

Okay. So they likely stack well together. And a pretty common side effect of Metformin is diarrhea. That's probably doing something to your gut bacteria. There's also studies showing that Metformin negatively affects mitochondrial function, which is one of the many reasons that I've decided it wasn't worth it for antiaging.

I've quit using it about seven or eight years ago for that. And if I had high blood sugar, maybe I would reconsider. But if your metabolism is working, I don't think it's worth it. If you can intermittent fast. Let's talk about intermittent fasting. How long of a fast is going to break my gut bacteria? And should I take Pendulum during an intermittent fast?

Colleen:

There have been said to have emerging studies around intermittent fasting and the effect on the microbiome. Typically, to have a longer lasting effect on your microbiome. It takes weeks or months to be able to do that. But the intermittent fasting, of course, you're significantly reducing the prebiotics and the foods that your microbiome is getting.

And so it's like an opportunity to have an occasional clearing out. And so it's the perfect time to introduce the right gut bacteria and the right prebiotics on the tail end of an intermittent fast.

Dave:

At the tail end, but not in the middle. Okay.

Colleen:

Yeah. I think it's the perfect time at the tail end, because you're clearing out the system and now all of your microbes are starved and waiting for what's the next thing that's going to come down the gullet and if the next thing that comes down, the gullet are the microbes that you want and the prebiotics that are going to feed those good bugs, you've kind of created the optimal system.

You can do it in the middle, but really when you think about it, if you are getting down to the minimal bacteria and they're all in a kind of a starvation mode at the end of your fasting, that's when you have the biggest chance to really change it like this. I'll just tell you, I don't take Pendulum glucose control in the evening and in the morning, I only take it in the morning.

Dave:

I think we talked about that on one of the other episodes that many different probiotics taken right before bed can affect sleep quality. Right? One of the things that's not well known, but is in at least a couple studies is that bacteria, whether they're in the gut or not have a circadian rhythm, just like people do. Which gee, our mitochondria are circadian based. They're the ones who are keeping the clock in the body. So this is one of the reasons jet lag. Even if you do everything else, right. It can mess up your gut bacteria, because they still think it's daytime.

So they're acting like it's daytime and probably talking to your mitochondria the way bacteria talk. If you listen carefully, you can hear them whispering. But there's stuff going on there that's meaningful and not well studied. But I have also noticed that I don't take any probiotics at night anymore. I take them all in the morning because that just seems better. I usually take them on an empty stomach though. If I take them, it's not really an empty stomach, because I'll take a prebiotics with them, but I take the prebiotics with no other food and no other... Like nothing else. That way there's plenty of fuel for these guys, but it doesn't change my blood sugar whatsoever.

Colleen:

Yeah. I actually do the same thing. So I start out the morning and all I take are probiotics and other supplements, prebiotics and things like that. And that's it. And then I don't actually have my first meal and of course, I have my coffee too. but I don't actually have my coffee-

Dave:

Prebiotic. Really.

Colleen:

Yes. It's a prebiotic. I actually have my coffee an hour after I take all those supplements and probiotics, but I don't have my first meal until usually lunchtime. It's again, this idea of, you've got everybody at bare bones and who are you feeding? That's who you're giving a leg up to.

Dave:

Okay. I like that. So that's real actionable for listeners. It's like probiotics in the morning, maybe at lunch even, but probably right before bed, isn't the best amount of time.

Colleen:

Yeah. I think for many people taking any probiotics, or prebiotics or supplements right before bed, does affect sleep.

Dave:

And that isn't I think well talked about and even in the world of biohacking. So that's a cool tip. And thank you for bringing that up. If you were completely given unlimited funding and you didn't have to worry about these pesky three letter agencies telling you that your natural compounds magically qualify as drugs because they said so, and they want to steal money from the US population.

Do you think you could engineer some kind of a gut bacteria that would just let us eat a lot more stuff than we do today and still be abundantly healthy? Like if the gloves were truly off?

Colleen:

Well, now you're really going to be recording me and getting me into trouble.

Dave:

This is science fiction. Like I'm saying, look, if you had unlimited money and people wouldn't tell you not to do stuff that as a molecular biologist, you're like, I think we should do that. What would be possible?

Colleen:

I believe. And we do work in this space and I think there's even larger opportunity that you can find bacteria or engineer bacteria. And we don't do any bacterial engineering. But I think that certainly can be done. You can find bacteria or engineer bacteria to help you metabolize pretty much anything you consume.

And I do believe that in the future, if anybody wanted to have an initiative to find or create bacteria that could metabolize anything that you consume, it can be done.

Dave:

Wow. So there will be biohackers around the world who are going to do that and it's going to enter their poop and the sewage system. And that's going to be part of our environment. It's just how it works. Today, for \$5,000 worth of gear, you can make your own bacteria that do different things. That cat's out of the bag. You cannot regulate it. People have been talking about even making their own viruses as individual biohackers for a long time. So there will be custom made gut bacteria and you may have to fly to another country that becomes enormously wealthy by being the place you go for that in order to get it. But I think it's probably already happening in military labs around the world. I promise you if they have a gut bacteria that lets you feed troops, even cheaper MRIs and still be healthy, they will be taking that probiotic.

It's just going to happen. Right? So I'm looking forward to a future where we say, okay, this is the easiest to change and modify part of our metabolism. So let's get to work on this. And you're at the cutting edge of getting to work on it. And you're taking natural strains that have unusual abilities that are not present in people and making them present, which is causing big changes in our biology, which is awesome.

And I just put on my 20 year hat and like, where are we going to end up with this? And I think it's going to be really, really cool unless this is one of those Bill Gates, nanobot gut bacteria controlled by Elon Musk's network of satellites that's influenced by both pyramids and aliens. Okay. You can tell, I'm not really believing that it's going to go dark. I also thought the internet was going to be used for enhancing freedom and access to knowledge. And it was for about 25 years. And then, you know, bad actors.

Colleen:

It's still sometimes in there and there will be bad actors. But a good thing about the microbiome is, when you want to think about what's going to happen in the future is sort of, let's go back to the past and why do we even have a microbiome? And I think at the end of the day, it's because evolutionarily, we by ourselves are not good enough.

And so these microbes that we've co-evolved with, not just in our gut, but also in our skin, in our nasal cavities, in our lungs. We co-evolve them because they're helping us be more efficient people. They're helping us have more efficient immune system, more efficient inflammatory responses, more efficient metabolism. And so when you think about that, these are really here to make us more efficient people. And you take that then to the future, then, you know the opportunity is limitless

Dave:

It is. And we're just to the beginning of the microbiome revolution. So I'm pretty excited about where we're going, just the amount of data gathering. And I appreciate what you're doing around saying, look, this is the lowest hanging fruit strain. And if you can just solve blood sugar control or at least help it, you get the longevity, you get the mental clarity, you get the mental regulation and you get a reduction in healthcare costs. So in my stilted view of the world where the money that we spend on our taxes is supposed to help people instead of fuel additional inflation.

Oh wait, no, that wasn't money we sent, that was just money the government stole with inflation. Anyway, they're supposed to take that and not put it in their pockets. They're supposed to spend that on things like this that would dramatically shift the health of the country in one year. If everyone had blood sugar regulation in their government funded probiotics, what would happen? We would see a collapse of the hospital systems because we have less people in the hospital. At least that's

what my data says. So like, this is all possible in the world we live in today with the knowledge we have now, when we have the willpower and the knowledge. You're sitting on a rocket ship there.

Colleen:

Yes. And I would say, in that vein, but maybe not quite so extreme. We made a very deliberate choice to not be a pharmaceutical drug and go down that path and instead to bring this product directly to consumers. And a big, big part of that decision was actually to enable people to go after preventative medicine. Because the healthcare system is not set up that way. You could only prescribe this product if you had type 2 diabetes, because that's what we did the clinical trial in.

But by making it available to consumers and everybody, that means that all the people who have prediabetes, who are worried about blood glucose spikes, who have diabetes that runs in their family. Now, all these people have access to this product. And at the end of the day, when we look at our customers, less than half actually have type 2 diabetes. And that is a big opportunity for the microbiome, is to create products that allow you to bring it directly to consumers and enable this whole concept of preventative health to actually happen. Because the only people actually incentivized to go after preventative health are us as individuals.

Dave:

It's exactly like that. We've got to do it. And our doctors aren't going to do it, except for a few of them. But generally that's not how the hospital system is set up. So kudos to any company who decides they have a product that people could just buy at a reasonable cost, or you could potentially make more money by turning into a pharmaceutical that's 10 times more expensive. And so I think the moral obligation is to make things available to people.

So I appreciate that I can buy Pendulum because it's my choice to do it. And I appreciate that you did really good clinical science so that I'm willing to do it. And of course, because you're a great person, you're giving listeners a discount because that's kind of the deal here. Pendulumlife.com, use code Dave VIP. And you're giving everybody a discount. Thanks for doing that for our listeners. And Colleen, thanks for doing Pendulum. It's a really cool company with really cool science. And I know it's hard to make what you make because it's anaerobic, but you did it. So congrats.

Colleen:

Thank you. And thanks for having me on.

Dave:

Guys, again, Pendulumlife.com, use Dave VIP, save some money and if you have a CGM and you're monitoring your blood glucose, you'll probably see a difference, if you try Pendulum. I certainly did.

Colleen:

Thank you.