Introduction to Gut Health and GLP-1

For this DrTalks, we are going to be exploring the connection between the gut and GLP-1. Joining me I have Dr. Adam Perlman, who is the Chief Medical Officer at Pendulum Therapeutics and formerly served as the director of Integrative Health and Wellbeing at Mayo Clinic Florida and the Medical Director for Employee Wellbeing.

Prior to that, he was associate V. P. for Health and Wellness at Duke University Health System, overseeing Duke Integrative Medicine and the Duke Diet Center.

Dr. Perlman received his B. A. from Tufts University and his MD from Boston University School of Medicine, completing residencies in internal medicine and preventive health, as well as general internal Medicine Research Fellowship at Boston Medical Center, and earned his master's in public health at Boston University School of Public Health.

Thank you so much for joining us, Dr. Perlman. it's great to be here. Excited to be talking about some of the Pendulum products and some of the science behind those products. And.

Well, let's start off with what that connection is between the gut and GLP-1 regulation. And even if you want to take a step back and explain the importance of GLP-1 as well.

Great. I'm glad you put that caveat in at the end, because I know you're obviously an obesity expert and and right for these medications all the time.

I don't know if this has been your experience, but it's been interesting to me, whether it's a patient or commonly, it's a friend or colleague that happens to tell me they're taking one of these medications.

And if we get into the conversation and it's not unusual that they don't realize it, it's actually, a hormone that they're actually injecting GLP-1, a synthetic form of this one.

And again, I say that without judgment. It's just interesting to me that people may know the name of the medication. They don't fully appreciate that it is actually a synthetic form of something that the body makes naturally.

And the body does this, really in response to a meal. And the way that works, the way that is signaled really works through the gut and the bacteria in our gut, which is sometimes referred to as the microbiome, this 70 to 100 trillion bacteria that live in our gut and in sort of a, let's say, a brief version of this, we eat a meal and, the specific strains of bacteria I'm sure will get into this later.

But specific strains of bacteria in our gut eat that meal, in particular the carbohydrates, the fiber, and they then release certain signals. Okay. They make what are called short chain fatty acids.

How Gut Bacteria Trigger GLP-1

They make some other molecules that bind to receptors on cells within the lining of the gut, these cells that are called L cells and those cells in response then release GLP-1.

And then GLP-1, of course, is interesting. maybe I'll just say this briefly. I was like this idea that, you know, we go and we fill our gas tank up and very often you can sort of click and it'll automatically start filling.

And just happened to me yesterday. And, you know, I can stop and look at my phone and check text messages while I'm standing there or wash the windows.

and then kind of by magic, all of a sudden the machine knows, the gas pump knows and click. It shuts off when the tank gets full. And of course, if it didn't do that, the gas would overflow and we'd have a problem.

And in many ways, GLP-1 works the same way. So we eat this meal. The bacteria in our gut sort of signal the cells in our gut to make GLP-1. And then in response, GLP-1 of course, goes and tells our pancreas to make our insulin, you know, tells our stomach to slow down the digestion so we can digest our food and feel more full.

And then of course, goes to our brain and, and signals us to feel full, stop eating so the tank doesn't overflow. And all of that is really the bacteria in our got this microbiome specific strains are really the middleman in that sort of, mechanism.

I, I want to go back to just one thing you said, which may not have been the most important at all, but you're I think the only person who I've heard kind of phrased this the same way that we're not just feeding ourselves, we're feeding this bacteria when we eat.

and I use that to try to convince my children they should eat their, their fruits and vegetables and their other whole foods, like, okay, okay, the bar is for you, but you got to eat some of those fruits and veggies to feed the bacteria in your gut, too.

So I think we, completely underestimate the role of our microbiome. We're kind of unaware that we have all these, like you said, trillions of organisms living with us that have such a huge impact on our health and, on on the hormones that are affecting our health and our appetite, as well.

So what are some of the key players in this gut GLP-1 relationship? Yeah. So there are a number of key players. They sometimes get referred to as keystone strains.

And this sort of comes out of really the advancement in science and technology with with technologies like PCR and sort of genomic sequencing that really allows us to better grow, study, bacteria that, you know, doesn't necessarily grow in a petri dish.

So let me step back to make sure I'm clear. Historically, when we think about probiotics, you know, people think about Bifidobacterium, lactobacillus, those may be names that are familiar to people in the audience.

And those are, strains that grow in oxygen. Right? They're aerobic. You could sort of put them out on a, on a dish within a lab, and they could grow. Some of the newer strains that have been discovered more recently are ones that can't be exposed to oxygen.

So they're not as simple. It's not as simple to discover for them to grow them, etc. and in particular, there are a number of strains, one being a strain called Akkermansia that was, let's say, discovered in 2004 that we now know has a really critical role in the body as it relates to maintaining our metabolic health.

it has effects on immune function, sort of maintaining a healthy weight and even even some associations with healthy, healthy aging. so that there's some Clostridium species, Clostridium bacterium being another, that, again, play this critical role within metabolic health and and overall health of us.

So, you mentioned that one Akkermansia, which I feel like I've been hearing, you said we've known about it for 20 years. I've just started hearing about it maybe in the last year or so.

Can you tell us a little bit more about that particular strain? And you know why it is so important, why it's getting so much attention? Sure. I'd be happy to.

So again, Akkermansia there the particular strain we're I'm talking about here is called Akkermansia muciniphila. So that's the full name for this one.

again really important role in the body. It's a gram negative bacteria for those in the audience who are interested.

but it, it does a few things and, and one of the key roles is related to metabolic health and GLP-1.

So I'll go just a little bit into the science here. But it makes short chain fatty acids in response to haven't eaten a meal, something we've just talked about.

Akkermansia and Gut Barrier Health

Again, those short chain fatty acids ultimately get converted to a short chain fatty acid called butyrate that then binds to these very specific G coupled receptors.

41-44 on these L cells stimulates the release of GLP-1. It also makes particular protein called P9. And that also binds to a different receptor on these L cells something called I came two for the for the scientifically inclined in your in the audience here.

But that also is a is a receptor that stimulates the release of GLP-1. It then has effects also on immune homeostasis or sort of the balance of our immune system.

That can be very important. But then the other role that I didn't mention yet is this role in helping to maintain the integrity of the lining of the gut.

So maybe I'll take just a moment to for those in the audience that are less familiar with how the gut works, if we think about the lining of the gut sort of single cells kind of line up, and as nutrients come by, the right things should be absorbed through the cells.

Sometimes things can pass between the gaps between the cells, called the tight junctions. And it's really important that that integrity, that lining is good, almost like a fence.

If we think of it like a fence, you want the boards to be nice and tight. You want in this case, this fence allows things through that should get in, but you really don't want to allow in the things that shouldn't. Okay.

And so you want those boards to line up. But there's also sort of a shellac along the outside of those boards that acts almost like flypaper, catching things that might be trying to get through the the gaps between the boards.

That shellac is called mucin. And so Akkermansia muciniphila is really Akkermansia mucin lover and what Akkermansia does as a part of its role is like a Pac-Man.

It sort of eats up old or degraded mucin and then stimulates a different cell in the lining of the gut, called goblet cells, to basically make new mucin.

So it keeps that mucin layer, it keeps that sort of flypaper, shellac, healthy and intact. The mucin also has an important role in helping to keep the cells that line your gut.

The internal sights healthy as well. And so in big ways, when we think about acromion. So we think about metabolic health. We think about, immune function, healthy aging.

And then we really need to think about maintaining the healthy integrity of the gut. I'll just add one more thing. As many of your listeners may be familiar with, when that integrity of the gut isn't good.

So when we have gaps between the boards of the fence or the mucin is degraded more than it should be, we can develop what if I want to some more like a doctor, I say increased intestinal permeability.

But what most people know of is leaky gut. And again, that can have a number of sort of downstream ramifications from a, from a health perspective. and then, there are other bacteria strains that we know are important in the, gut GLP one relationship.

Yes. I mean, I think it's important to recognize, you know, trillions upon trillions of bacteria, thousands of strains. we've evolved to really live, synergistically with the bacteria.

Now, we couldn't live without it. They couldn't live without us. And there's a lot of overlap in in responsibility, let's say. And there's bacteria that support other bacteria while they're doing their job helping to feed those other bacteria as well.

So there's many, many strains. the ones that I like to emphasize, the ones that that pendulum studied, in addition to Comanche and sort of brought to the market, was, some, Clostridium strain.

So at Comanche was the big one. But some stadium strains can be very important. I think a good example would be something called Clostridium butyric. again, a number of different roles in the body.

But the key role here as it relates to GLP one and metabolic health would be the release of butyrate. Again, we've been talking about beta eight, the short chain fatty acid that then binds to these this receptors on the L cells and then stimulates the release of of GLP one.

There is a second mechanism I'll mention again, which is interesting. Clostridium also helps to convert what are called primary bile acids to secondary bile acids.

These are things that the liver the gallbladder makes. but they also have a role. So, there's a secondary bile acid called udca that Clostridium as a bacteria helps to convert and make.

And that actually binds also onto the L cells and helps with the release of GLP one. And so through releasing butyrate, through helping to create more udca in the body, Clostridium really does, again, you know, play an important role in, in our body's natural ability to release GLP one.

I think you're doing a nice job trying to highlight how complex all of this is, which is why, you know, we've we've known in a lot of ways that the microbiome is important to our health and that, cracking certain things or treating certain things within the microbiome is probably a huge part of the future of medicine.

At the same time, it's like immensely complex, right? It's like this whole ecosystem, inside of all of us. And, so, you know, I think in some ways, because I, you know, I've been watching this my whole career, like the progress sometimes seems a little slow with how we translate what we know to things that actually impact people.

Because, again, it is so complex. You have this gut microbiome, which is basically a whole ecosystem inside of our bodies. But then we have all these hormone relationships and other relationships within the body as well.

And so, really, although we know it's been important for quite some time and we know it's having huge impact on our health and our metabolic health and all these things really, you know, haven't had the opportunity to see a lot of this translate into things that actually change people's health because, again, it is so, so complicated.

Other Key Microbes and GLP-1 Support

So, with all of that in mind, can you talk a little bit more about the role of using probiotics, prebiotics? in order to try to, you know, change metabolic health and improve cravings and help with satiety or that fullness feeling.

Yeah. So you, you know, you you bring up a really important point. I mean, this is a complex ecosystem, right? It's not as simple as, you know, I just drop a little bit of probiotic in and, and all my problems go away.

Or even understanding sometimes how all these things interact is, is something we're still unraveling. I mean, it's really one of the next great frontiers of our understanding of health and how to influence health in a positive way.

That being said, what is exciting to me, what was exciting to me when I when I came to pendulum, just a short while ago, from Mayo Clinic, was sort of the way that the science was advancing and how there was a newer

sophistication to our ability to make recommendations around probiotics.

Again, historically, most of the things being on the market kind of Lactobacillus, Bifidobacterium type species. But now you have a company like pendulum bringing this very hard to grow, bacteria, that are, you know, anaerobic, can't be exposed to any oxygen.

But here it's now available. and we're understanding that it along with other strains, it has really profound effects on human health. And so, What what we found is that often it's important to take a combination of probiotics together and know that you're taking the right strains for the right particular indication.

So if we're talking about something like satiety and cravings, because I think that's what you had asked me about, that's a great one to focus on. And I'd make a couple of points.

One is that so often I know in my practice, I would imagine in your practice or just in our lives, you know, you have people that might be struggling with maintaining a healthy weight, struggling with cravings.

And, you know, often it can be so difficult and people can feel guilty, you know, feel like, why am I not able to kind of get this under control? And a lot can be going on there, of course, but very often it may be that there is, you know, a relative deficiency or imbalance in some of these really important bacteria in our gut.

And so in some ways it's kind of not our fault, if you will. and, you know, we're just needing to find ways of addressing that imbalance. And that's where some of these probiotics come in.

And so one of the things that that we did at pendulum is we took, this three strain formulation that now is on the market as GLP one probiotic, but it has the acronym Nancy, a mucin Ophelia that I was talking about, the Clostridium butyric, and then a Bifidobacterium infantis, which is another strain that again, if your listeners are familiar, if listeners are familiar with, you know, the microbiome at all, that's as the name sort of implies, one that we think about more early in life in infants, but it continues to play an important role.

And that's actually what's called a primary. It's actually a primary fermenter.

Probiotics, Cravings, and Satiety

So it ferments complex carbohydrates, basically makes short chain fatty acids, things like acetate and lactate that are a fuel for the other bacteria.

So the again I said this earlier, but these bacteria sort of work together. So in this case we took this three strain formulation. And we did a consumer study where we actually, gave it to 274 individuals over a three month period.

And what we found interestingly, was that at six at six weeks, 91% of the individuals involved in this consumer study had significant reductions in cravings.

I can think I can say this. We're still finishing up the analysis, but I think I can say that at three months the number was 93%. So at three months, 93% of participants experience reduced cravings.

And what was interesting is, that what we saw was that the higher the individuals cravings at baseline, the greater reduction. So if you had more cravings, you seemed to feel, you experienced a greater reduction in those cravings and that the cravings, pardon me, were really across all four areas at this particular questionnaire I looked at.

So it was, sweets, sugars, basically carbs and starches. fast food fats and then high fat foods. So across all of those categories, this particular, questionnaire looked at, there were, you know, significant, significant amounts of people experience reductions in cravings.

So 88%, if I'm remembering correctly, 88% of individuals experienced a reduction in cravings for sugar, for example. And so, you know, this is, I would say, simply by giving the right bacteria to individuals who apparently,

you know, without even being aware of it, had some sort of imbalance, you know, it appears, or a deficiency in some of these strains.

I mean, these strains clearly had a positive beneficial effect on their cravings in this particular study. and interesting that it helps with all the different types of cravings, right?

Because some people when they I always try to figure that out when someone comes in to see me, like, you know what do they struggle with? I always try to figure out why they're struggling with their weight, what their cravings and, and other reasons may be.

And people be like, oh no, no, I don't have a sweet tooth, you know, but like, oh, fast food. Like, I feel like I'm addicted to fast food. Right. And so sort of if you're that person who is driven by any sort of craving, it sounds like, reduces sort of all cravings.

It's not just for the sweet tooth people or the the fat food, fast food people, really any sort of cravings? It seems to help with it. Yeah. It was interesting to me.

I mean, I hadn't done, research using this kind of questionnaire before, and it was interesting that they did split the cravings into different types of cravings.

And of course, you know, we all know we all have our particular vice. and, yeah, but across all these four different categories of cravings, we saw, you know, a robust response in terms of, of cravings and, and feeling more full.

That was the other thing. And then at of curiosity for the people who were in this consumer study, were they told to do anything different in terms of what they were eating or, or just to take the probiotic and live their life and, and see what they experienced?

Yeah. Great question. In this case. No, we just added in the probiotic and we did, you know, at baseline, six weeks, three months to see what the effect was.

And of course, you know, we do know things like changing your diet can be very important. But in this case, we were trying in this consumer study just to isolate the probiotic itself.

And as I think I mentioned earlier, you know, we'll be following up with a more robust clinical trial. Very cool. Yeah. So because, you know, if you were like adding in a different diet, that could explain some of it, but they were just continuing on with with what they were eating and then seeing if they had less cravings.

So that's pretty cool. so we'll look forward to that. That clinical trial. so from the nutrition standpoint then what do individuals who are, you know, looking for the most benefit from these probiotics need to be thinking about what can they do to also help support their gut microbiome?

Yeah, it's a again, a great question. And in my clinical practice, I mean, it's unusual that I would simply give someone a probiotic. I mean if particularly if their, their, their goal is to, to, be at a healthier weight or manage their cravings.

Obviously we're going to be talking about nutrition. And I often think about that in sort of two main categories of what you don't want to be putting in there and then what you can put in.

So what do we need to remove from the diet, let's say, or at least limit in the diet that may be having a negative effect on the, on the microbiome. And you know, by and large that would be things like sugar and highly processed foods.

I mean, things that most of us that have, even a little interest in nutrition are fairly aware that probably not good for you. but it may be even things like Diet Cokes or diet sodas, I should say, or, you know, other things that, you know, overall can have an interaction with the microbiome that that may lead to some negative ramifications in

certain individuals.

And this goes back to sort of the individuality of how we might respond to even different dietary interventions. But I think, you know, those, as a general guideline, less sugar, less processed foods.

Diet, Fiber, and Polyphenols for Microbiome Support

And then on the other side of it is really making sure that we're getting enough fiber in our diet in many ways to do that, either through diet itself or certainly supplementation.

And the final would probably be polyphenols, which we get from, you know, berries and, and other sources, actually many sources, herbs, actually, cloves is probably one of the number one source of, of polyphenols, cyber and polyphenols really can feed the healthy bacteria with, polyphenols.

There's also a very interesting mechanism where it actually there's some evidence that polyphenols inhibit, to a certain degree, the enzyme that kind of breaks down GLP one.

So at least potentially leads to more GLP one floating around, let's say for a longer period of time. and so that's also a very interesting mechanism.

And these are things that have other positive health benefits as well. And of course, if you're having difficulty, getting that through your diet, you can supplement pendulum actually has an excellent polyphenol product where we actually developed it from specific polyphenols sources like green tea and pomegranate, to and grapeseed that we actually studied to to determine what said the particular strains that we've put on the market the best.

And so that's another option for someone that may have difficulty getting the polyphenols through their diet. you know, what you said about watching those processed foods has to be the most consistent messaging I have heard.

And I pointed this out a few times throughout the summit after, you know, interviewing about 40 different experts in this process like that has been said by so, so many of you.

So I hope that's a huge highlight for people listening is that, you know, we have to feed our body and our gut the right stuff for someone who is trying, maybe any probiotic, but specifically, the GLP one, product that pendulum has, how long should someone be expecting before they see results or know if it's working for them?

How long do you recommend someone you know maybe take it before they say it is or isn't working for them? Well, again, both. What I've experienced in my clinical practice and and what we've experienced in the research that we've done, it can be variable, of course.

it can take some time, but some people will experience changes, very quickly within a matter of days. but I usually recommend give a trial of up to three months.

I mean, even in the most recent consumer study we did with the GLP-1 probiotic, as I've said earlier, that 91% of individuals had experienced something within six weeks and that bumped up to 93 by three months.

But I, I feel, you know, a three month trial is a fair, a fair chance to give, the probiotics to work. Or as I said, but in my experience, the majority of people will notice a response prior to that.

And then I guess also along with that, is there any, you know, like safety or, you know, other concerns people need to be aware of if they're considering taking it?

Yeah. I mean, these probiotics like most supplements, are generally recognized as safe grass. So I mean, again, by and large, you know, these are very safe things.

I always encourage people to discuss their use of any dietary supplements with their health care providers. Of

course, that's very important. I think the main thing that we see is that, like anything and this is impacting the microbiome, but like anything we take, you know, you can have, side effects.

again, overall, this both anecdotally and from our research, you know, these products are very safe and well tolerated.

How Long Probiotics Take and Safety Considerations

I would say the most common side effect that people experience will be a GI side effect. You know, they may notice a change. Again, I sometimes I'll recommend in my practice they try cutting back, you know, maybe the gut wasn't quite ready for a pill a day.

Maybe try a pill every other day. and see if you you just need to build up a little bit. Very often, if people give it, you know, 5 to 7 days, whatever the, you know, GI related side effect, if they're getting a little bit of bloating or whatever that may be, tends to to resolve.

but there's always those individuals, like with any natural product or medication that just don't necessarily tolerate them. Unfortunately, with a product like this, you know, that's that's, you know, definitely the exception that the people don't.

I think, you know, I kind of think of, the microbiome and taking probiotics a little bit like gardening, which I'm actually quite bad at. So maybe I shouldn't make this analogy, but, you know, you're you're growing something, right?

And so you may not see something immediately. just like, you know, if you water your plants a little bit more, you're not going to see a change the next day.

but you're over a period of time going to, you know, see that change. and then if it's me and your plant is just brown and dead, like at some point you might just have to give up and say, you know, the water is not going to solve this problem.

But but we are growing something. Right? And so, you know, you're going to have a little bit of time and there may be some adjustment to your body to as you're, you're trying something new.

but unless it's really significant, like we are changing gut microbiome, like we're going to expect some changes in our gut. I think, you know, that's a great analogy.

I've I've used it myself in the past as well. I would even take it to the point of in some individuals, maybe you need to work on the soil first before you actually throw in more seeds.

And in this case, that might be individuals that might need a period of a low Fodmap diet or some other work on their gut before they're ready for that reintroduction or that introduction of the probiotic that's really in discussion with your health care provider that kind of knows, gut health and can help guide you.

And I think it's also important to recognize, you know, this is all about taking the right probiotic in this case for what your particular goals are. So, you know, we've talked a lot about GLP one, but it's a great product.

It's you know, particularly if you're looking to manage cravings and satiety. we actually have the Pendulum. Glucose control is a product that we did a randomized controlled trial that was published in 2020 actually in type two diabetic diabetics with metformin.

So if individuals that already have, you know, type two diabetes, clear signs of of, you know, more advanced metabolic dysfunction, you know, there's a five strain formulation that that we've shown can be very helpful in those individuals.

Very cool.

Choosing the Right Product and Closing Remarks

Well, Dr. Perlman, thank you so much for joining me. really cool to see the science that's being applied here. if people want more information, where can they go?

You know, I think these is just go to our website pendulumlife.com. pendulumlife.com. And you know, not only is there obviously they can purchase the products, but we have a lot of resources there.

Information I know some of the audience or health care providers, we have protocols for health care providers. If you know what, if someone has low Akkermansia, what what might we do then?

And then? You know, there's other information that, you know, either a health care provider or the public would find helpful. Wonderful. Well, thank you again so much for for joining me.

Thank you so much for inviting me. I really enjoyed it.