Butyrate also plays an important role in metabolic control by stimulating the secretion of the gut peptide, glucagon-like peptidone, or, you know, GLP-1, which is a very hot topic in metabolism today, given drugs like, Wigovia and other drugs that are getting really dramatic results.

GLp-2 secretions is known to be decreased in patients with type 2 diabetes. This is Doctor Talks. Hi, everyone. Welcome to the Reversing Type 2 Diabetes Summit.

I am your host, Dr. Beverly Yates, MD. It's my distinct honor and privilege to interview Dr Orville Kulterman. He's a wonderful expert who has been a key part of the team at Pendulum who's been developing these marvelous therapeutics that are probiotics-based.

He's the chief medical officer at Pendulum since its launch. He is also an adjunct professor of medicine at the University of California San Diego. Yes, a successful and distinguished 40 year medical career.

And during his 20 year tenure at Amalin, he served as the Chief Medical Officer. They are creating two of the first GLP-1-L drugs, Simlin and Bayetta.

We all know that these peptides that are so powerful are really making a difference for people who are just struggling, struggling struggling with their blood sugar.

Before AMLIN, Dr. Kulterman was the program director of the General Clinical Research Center and medical director at the University of California Medical Center.

With that, we say welcome to you, Doctor Kolterman. Thank you for having me. It's really a pleasure to be here. I look forward to the discussion. All right, great, so we're gonna be talking about the gut's microbiome and using that as a targeted tool for glucose management.

And when we were looking to control blood sugar, I think people often don't connect the dots around the health of their gut and its microbiomes and how profoundly it can affect bloodsugar and glycemic control.

We're going to definitely unpack that here in this discussion. Right, look forward to it. Okay, so we all know that for a long time, for quite a number of years, that the access, the connection between the gut and the brain has well established.

Lots of research, lots of clinical experience, and lots lived experiences of people who've gotten better as a result of that work. So how did you know to explore the Gut for Answers to metabolic diseases like type 2 diabetes?

Also, the story begins with the coming of the general or detailed genome sequencing becoming available or actually becoming cost-effectively available.

With that, academic investigators began looking at what was in the gut, knowing at the outset that there was millions of bacteria in there, but understanding whether they were the same in every individual.

more importantly, whether there were any associations with disease states. And so, early on, those investigators began to notice that certain diseases were associated with specific profiles within the microbiome.

And as it relates to type 2 diabetes and the metabolic syndrome, there was decreased diversity, which means that there weren't as many members of the community as you saw in healthy individuals.

And also in a particular importance, There were two classes of bacterial functions that were sorely underrepresented in those microbiomes. namely the ability to produce short-chain fatty acids.

And then the other is to maintain the gut barrier that keeps things within the Gut Lumen, the various toxins and what have you that You know, evolve as food is digested and other events happen in the GI tract.

Number of those substances are toxins if they get into the bloodstream and they generate inflammatory processes. So it. there was an association, but that just represents, at the outset, that's guilt by association.

So that does improve causality. And so the next step was, and as it relates to metabolic diseases, particularly type 2 diabetes, We were well positioned to delve into that because there are multiple well-established, well characterized rodent models for the disease.

So these observations were taken into those rodents models. I guess the most straightforward way to talk about it is that there were feces where our tickle samples were harvested from patients with type 2 diabetes and then transplanted into one of these rodent models.

And it was observed that even if you did the transplant into a healthy, quote, normal mouse or rat, that rodents, you know, eventually developed type 2 diabetes, became obese, insulin resistant, and hyperglycemia followed.

It was also in those models, it demonstrated that if he took, if did a maneuver that restored the normal composition of the gut microbiome that the disease went away.

You could do that by transplanting a fecal sample from a healthy, lean human or the things that we associate in clinical practice that tell our patients that they should be doing or if they can do them, they will be beneficial in terms of managing the Namely, increasing the fiber content of the diet.

So in these rodent models, it was shown that if you put soluble fiber into the dietary animal, that the microbiome would be back to normal. And the other thing was that, if did a transplant from healthy rat into a diseased rat, you could also ameliorate the disease.

Okay. Okay, so I've always thought those particular experiments and research has been fascinating to me. And I have heard of it being done for type 2 diabetes.

I heard it been done obesity and also when people have really, really nasty GI illnesses, like say they have an infection with T. difficile, you know, Clostridium difficile bacteria.

I think it was amazing that people came up with the idea of a fecal transplant. To me, a faecal transplant is not the most obvious therapy, but it has given some profound insights to the power of that gut microbiome for sure.

That's absolutely the case, and we now understand that there are these dysbiosis or abnormalities of the composition of a gut microbiome across the whole spectrum, you know, of diseases, neurodegenerative diseases.

You know nash dappled, the fatty steatosis or fatty liver disease, cardiovascular disease. Depression, and the list is just growing, ever growing even today.

It is amazing how this list is growing and we're all working. The work you're doing there at Pendulum, the work I'm doing, our other colleagues are doing.

We're trying to turn this trend around. Okay, so with that in mind, what are the two main dysfunctions that can occur in the gut microbiome of the people who have type 2 diabetes?

Well, two major dysfunction are production of short chain fatty acids. Let me digress for just a moment. I mean, when I was in medical school, basically learned that the GI tract was sort of a tube through which food passed and some of it was absorbed, but the fiber content of the diet was largely unobsorbed and unaccounted for.

But it turns out that that fiber, when it reaches a colon, is the food stuff or a healthy microbiome. And the microbes, as they digest that fiber, they produce short chain fatty acids, acetate, tropionate and most importantly, butyrate.

These short-chain fatty-acids nourish the lining of the gut and help maintain that gut barrier that I mentioned but they also can pass into the bloodstream and serve as messengers to the brain, to heart, various parts of the body.

And then butyrate also plays an important role in metabolic control by stimulating the secretion of We've got peptide, glucagon-like peptidone or GLP1, which is a very hot topic in metabolism today, given drugs like Wigovia and other drugs that are getting really dramatic results.

GLp1 secretion is known to be decreased in patients with type 2 diabetes, and so increasing the production of butyrate can help reverse that deficit. The other major defect is what can be discussed under the umbrella of a leaky gut syndrome.

So it mentioned how the short chain fatty acids are nutrients for the lining of the gut. That keeps the cells of interstitial lining healthy, but It also helps maintain the tight junctions between the interstitial cells, which is a major component of the system that blocks toxins from entering the bloodstream.

The second component is that on top of that the the intersectional lining of gut, there's a layer of mucin. that also serves as a barrier. And patients with type 2 diabetes, that mucin layer thins, and in some cases, it can almost be, you know, non-existent.

Those combined, the thinning of the muccid layer, unhealthy lining cells, loosening of the tight junctions, you know, allow various toxins to enter the bloodstream.

And we now understand that those toxins create an inflammatory state almost anywhere that you want to look in the body. It's become to me understood or it's been demonstrated that there is inflammation in skeletal muscle and adipose tissue, which is particularly important in type 2 diabetes because it may be the major driver of the insulin resistance that has been known to be associated with type two diabetes for some time.

So you need those functions to be present and robust in order to have a healthy gut and avoid this leaky gut syndrome. Makes sense, it makes sense. These things are all a partnership and they work together.

That's for sure. And some of us, that kind of basic health has been completely undermined. So we can see now why people would have problems with their blood sugar regulation.

Okay, so with this in mind, these two main dysfunctions that occur, are there specific bacteria that are decreased or missing in individuals with type 2 diabetes?

And if so, what made them go missing? So there are two strains of bacteria that are particularly important that our decreased or absent, sometimes absent in patients with type 2 diabetes.

One is there are multiple strains with a form of cluster of butyrate-producing bacteria. We just talked about how butyrite is important. So those strains, particularly C.

butericum or Clostridium buterycum being decreased or absence, results in decreased butylate production. And then all of the things that butorate does sort of fall in disrepair.

The other sort of hallmark strain is the strain Acromansia mucinophilia. This is a bacteria that actually lives in this mucein layer that I described.

And this bacteria was first described in 2004, and it's been fairly intensely studied since that point in time. It's now known that it plays multiple important functions.

It actually eats, it actually lives off of the mucin layer. Now that seems like a dichotomy here. So we need a healthy muccine layer, but now we have an important bacteria that is eating the Mucine Layer.

How can that be? Well, It's becoming pretty clear that the way this works is that that bacteria eats damaged mucin.

It's mUCin that is aged, it's been, if you say, beaten up in the battle.

And so it clears out that damaged, you know, mUcin and by so doing, that actually stimulates the proliferation of goblet cells within the interstitial lining.

These goblets cells are the cells that make mucin. So you get an increase in the number of cells and you also get and increase of output of muccin, you know, by those cells.

And that is the way that the muss layer is replenished, and maintained. After mancia plays a very important role in regulating that process. Oh, super cool.

Good to know. It's interesting how important it is that the body have places and ways, processes to regenerate and restore. And I did not know that mucin was impacted this way with the cobalt cells and all.

So that's a key piece of that journey to understand, particularly if you're a health professional, a medical colleague, etc. So for those of you listening to this episode, you know, take notes because you might be getting some insights on information on how this all works that perhaps aren't common knowledge.

Okay, so with that in mind, go ahead. There's one other thing to add about acumencia that I failed to mention and that is that It has been demonstrated to be a really powerful stimulant of GLP-1 secretion, you know, itself.

It actually secretes a peptide that stimulates GLp-2 secretions. There's another peptides that's part of its outer wall that when the outer walls break down, it's released, that stimulate GL-P1 secretion and then it actually secrete sort of endocytoplasmic vesicles.

that can also stimulate GLP-1 secretion. That's great. Powerful to know. And a lot of people are talking about these GLp-I receptors, the actual biochemistry, and the medications that impact it.

So now we have something that's more natural that also is clearly a powerful player there. It's just great to now. it's always interesting to me that some things are just almost like a power intersection, a nexus of things in the body where if we can affect that, we could have marvelous change, positive change.

Absolutely. So you also asked how did this go astray? How did it go off of the rails? Well, the Western diet is heavily implicated in this. So if you think about what characterizes the, you know, Western Diet, it's rich in simple sugars.

It's depleted of complex carbohydrates and increased fat and protein. approach to starving the microbiome. And so that starvation situation that is set up leads to multiple bacteria sort of saying to hell with this, I'm not going to hang around here anymore.

They leave the community and as they leave their function, they also leave with them. The microbiomes is actually It's more than a village, it's actually a well-integrated community where, you know, microbe A does its thing, but it produces products that help micro-B either do its job or actually serve as nutrients for the microbiome.

And so you have to have all of the players present, all the functions represented to help a healthy microbiomes. That totally makes sense, there's synergy here.

All right, so then is there evidence for the use of probiotics and prebiotics in glucose management in individuals with type 2 diabetes? Absolutely. So it turns out that the time-honored recommendations that dietitians make to patients with type 2 diabetes, one of the reasons why they enjoy the success that they enjoyed is that replenish the fiber content of their diet.

So they're putting the food stuff back in. to the gut to feed a healthy microbiome. Probiotics, at Pendulum we formulated a live stream probiotic that also has a bit of a prebiotic inulin in it.

And in a controlled clinical study, we demonstrated that just simply adding that to the patient's daily life practices, you know, no further dietary modifications or anything resulted.

So this study was done in patients who were treated with metformin but were not achieving the degree of control. that was desired, and when this probiotic that's now sold as penulin glucose control was added into the regimen, it resulted in a mean reduction in A1C of 0.6%, 0,7%, and also it achieves that primarily by reducing the surge in glucose that follows the ingestion of a meal, the so-called postprandial spike, And that spike was reduced by 33%. And so that resulted, you know, knocked on into the reduction in hemoglobin A1C and improvement, of the metabolic state of, the patients.

Now this change was associated with an increase in measurable butyrate within the stool. And it also correlated to an increased in butyrite within plasma.

And when you will get the. increase in butyrate and plasma and correlated with the change in hemoglobin A1c, there was a direct correlation so that the greater the increase and butyrite, the great of the reduction in, in haemoglobulin A-1C, which does a very nice job of tying all the animal work related to type 2 diabetes together with what is seen in the clinic.

And it, so it just reinforces the importance of a butylate pathway. This all comes together, doesn't it? The integrity of the gut and the guts lining and all the beautiful things that our digestive tract does for us are really critical to our health.

And for blood sugar regulation, this is an important point that I feel overlooked. So I'm really glad we're doing this interview. That's for sure. People I am hopeful are getting plenty of insights and maybe reaffirmation of this central role that the Gut plays in determining blood, sugar and metabolism.

Well, that's a very, very important point, and it's something that didn't exist. It's knowledge that did not exist when I was in medical school. Okay.

So, from a nutritional standpoint, is there anything that individuals with diabetes can do to improve the state of their gut microbiome? So the important thing is to pay attention to the fiber content of the diet, particularly soluble fiber.

So where does soluable fiber come from? Well, it comes from fruits, especially blueberries, strawberries, any berry is good for your microbiome. Vegetables such as broccoli, cauliflower, spinach, Beets are good sources as are whole grains, quinoa, chia seeds, nuts, particularly almonds and walnuts are a good source.

unrefined flowers, like whole wheat flour, oatmeal or oat flour. Those things also have good fiber in them to nourish the microbiome. Okay, so it sounds like there's lots of opportunities to replenish and restore and help that gut to heal.

So I think in today's world, where many people have an amazing exposure to highly refined foods, ultra-processed, low nutrient density, strange chemical additives to stimulate the appetite and tongue, etc.

that it's kind of an uphill battle from a nutritional standpoint to stay healthy and well, and certainly to protect the integrity or restore it of the guts microbiome.

So the products that Pendulum has formulated are key to addressing that issue. Yeah. One way of looking at what I've described here is that if you do the dietary practices, you get benefit from it, but that appears to be sort of half of a loaf.

If you combine that with the probiotic, in and of itself helps put the healthy bacteria back into the gut microbiome. You actually get nice synergy and you get a larger effect.

Great. That's so good to know. Before we end our episode here, our interview, I'd like to if there's a place where people can get more information about this.

Sure. If you go to our website, which is BendulumY, all one word, pendulumlife.com. The products are available there, but there's also a lot of good information about the science.

There's a special landing page there for healthcare professionals where you can find various white papers addressing various topics related to the microbiome.

Okay, great. So while we're here, I want to be sure we can capture this website address is PendulumLife.com. Right. That's P-E-N-D-U-L- U-M- L-I-F- E dot com.

Is that right? Correct. Okay. Great. All right. Some friends as you watch this episode, particularly our colleagues here. Health professionals, please share this with others so they too can benefit.

And anyone who's watching who is a member of the general public, I'm sure there's some information we just shared here from Dr. Kolterman's insights that are probably news to you.

Think about what's going to be supportive and help you in your health journey. You're welcome to make use of these products and find out what the benefits could be for you I think that as we go along, there'll be more in the way of personalized medicine with really specific targeted results.

because we all know that people don't respond identically to everything in their environment. And nutrition and stress and life and all these other things impact us the same way.

So as you put together what's working for you, we invite you to be a part and you make use of the pendulum product. Thank you for tuning in to Doctor Talks.

We hope today's episode has enlightened and inspired you on your path to optimal health. Each day is a new opportunity to make choices that empower your well-being.

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