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How Diet Can Affect the Gut Microbiome

Dr. Buse:
Welcome to *Diabetes Discourse* on ReachMD. I'm Dr. John Buse. And joining us for a discussion on the gut microbiome and how it can be affected by diet is Dr. Karen Corbin. Dr. Corbin is an Investigator at the AdventHealth Translational Research Institute in Orlando, Florida.

Dr. Corbin, thanks for speaking with me today.

Dr. Corbin:
Thanks so much for having me.

Dr. Buse:
To start us off, Dr. Corbin, can you tell our audience a bit about the gut microbiome and how it may be involved in health and disease?

Dr. Corbin:
Yeah. So the gut microbiome is a term that describes the trillions of microbes that live in and on the body, and most of those reside in the colon, and most of those species are actually bacteria. So a large body of evidence both in mice and other preclinical models and in humans shows that these microbes are not something to be feared but something that performs very important functions for the body, like improving immunity, communicating with organs and the host such as by releasing hormones or proteins, and also perform fundamental functions in taking energy from the diet and making it available to the human host. So overall, it has been shown that the gut microbiome could be associated with many diseases, including diabetes and obesity.

Dr. Buse:
This is such a hot topic. I saw something in the press today about the link from the microbiome even to Alzheimer's disease. So with the background that you provided, how did you design your study to learn about the role of the microbiome and energy balance?

Dr. Corbin:
I'm so excited to tell you about this, and first let me say that this was a really unique collaboration between AdventHealth's Translational Research Institute bringing together our expertise in precise phenotyping and deep phenotyping of human metabolism and Arizona State University's expertise in microbial ecology. Advent Health's team was led by Dr. Steven Smith, and Arizona State was led by Rosa Krajmalnik-Brown.

So when this study was conceived, one of the biggest missing links in the literature about obesity and the gut microbiome was causality. So are the microbes actually directly impacting somebody's body weight, or are they simply a reflection of the conditions of the human host at the time that you take that measurement? So we realized that there's a couple of gaps we needed to address in our design. Number 1, it was that we needed a precise quantitation of the entire energy balance equation from intake to expenditure to fecal energy loss, and number 2, that we needed precise and deep phenotyping of both the host and the microbes—and here's the most important part of this second point—under strictly controlled conditions of diet and environment.

And so we designed a study with a couple of key elements to achieve these goals. First, this was a controlled feeding study, meaning that all the foods were prepared by our metabolic kitchen, they were provided to the participants, and they consumed them at home; and then during the measurement periods, they actually lived with us in our metabolic ward, so they were observed; adherence was nearly a hundred percent because we kept track of everything. And that's a really big difference between our study and studies that rely on someone telling you what they ate or somebody being educated to eat in a certain way.

The second important thing is that this was a randomized crossover study. This means that each person received two diets in random order. And this is critical because this allowed us to have every person serve as his or her own control, which is fundamentally important because everybody's microbiomes are so different. So our main goal was to reprogram or modify each person's own microbiome with two different diets. One was a Western diet, and one was what we call a Microbiome Enhancer Diet. The Western diet is kind of what you'd imagine, sugars and not a lot of fiber and a lot of processed foods, but the Microbiome Enhancer Diet was the total opposite, and it had four key drivers. One was high in fiber. Two was the inclusion of foods with resistant starch. Resistant starch is a type of starch that escapes digestion in the upper GI and makes it all the way down to the colon where the microbes can access those starches and ferment them. The third was to include foods with higher sizes of pieces, basically larger particles, and the reason for this is the larger a particle is when you put it in your mouth, the more likely some of that ends up available to the microbes and less available to us, which is an advantage, and we also limited processed foods. So with these two diets, we were then able to precisely quantitate the energy balance equation and look for differences in energy balance.

A couple more key points is that we fed everybody exactly the number of calories they needed, and I can say exactly because we knew how many calories they needed because we measured that in our Whole Room Calorimeter. And second, and this is also very important, these diets differed just in those four drivers I mentioned. Otherwise, they had the same amount of carbohydrate, protein, and fat. So the main difference was how much fermentable dietary substrate or dietary components were available for the microbes so that they could use them, and then we can measure the difference between someone that has a gut microbiome that's essentially starved and someone that has a gut microbiome that's getting plenty of food.

Dr. Buse:
We don't have time to go over it all, but can you give us the top line of the important findings that you had?

Dr. Corbin:
Yeah. So under these conditions that I just described, the main finding was that when people eat the same number of calories but one diet feeds the microbes and one diet starves the microbes, on the Microbiome Enhancer Diet that feeds the microbes quite adequately, people lost a lot more calories in their poop, an average of 116 more calories lost in the poop every day by people who ate the Microbiome Enhancer Diet compared to the Western diet. Now 116 calories maybe doesn't sound like a lot, but think about how many calories that would be in a year and how that could add up to be impactful for body weight. So that was sort of the top-line finding, and that was accompanied by a few key points. Number 1, people did not burn more calories. There wasn't higher energy expenditure. And people also didn't also have differences in hunger or fullness, meaning that even though we had this negative energy balance on the Microbiome Enhancer Diet, at least within our conditions and our sample size we didn't see them being more hungry, and this could be advantageous because the worst thing about trying to lose weight is feeling restricted in what you can eat and being hungry and wanting desperately to eat more. So if this translates to, larger populations where we focus on measuring this appetite component, it could mean that there could be a distinct advantage for weight loss, not just in the negative energy balance but in people's ability to maintain caloric restriction because they don't feel as hungry.

We also found certain hunger hormones or satiety hormones were higher on the Microbiome Enhancer Diet. And importantly, this is the question I get a lot. Isn't this just about that people pooped out more of the undigested fiber and that's the energy that you're measuring? And the answer is it is part of the energy we're measuring, absolutely, but we know that the energy was also used to grow the community of microbes in the colon, so the population expanded. This population is called biomass. So we know a significant proportion of the energy that was lost on the Microbiome Enhancer Diet was used to grow a larger biomass of microbes that were capable of fermenting some of the foods they received.

Dr. Buse:
For those just tuning in, you're listening to *Diabetes Discourse* on ReachMD. I'm Dr. John Buse, and today I'm speaking with Dr. Karen Corbin about the diet and the gut microbiome.

Before the break, Dr. Corbin, you were telling us about the greater fecal loss of calories and change in microbial metabolites without changing energy expenditure, appetite, or satiety associated with—I think it was about a pound of weight loss—with the Microbiome Enhancer Diet. Is this something that's ready for incorporation into dietary recommendations?

Dr. Corbin:
Yeah. So you're right, John. I didn't mention that even though we tried really hard to keep people in energy balance and by every measure known related to human digestion, absorption, and energy expenditure, we absolutely had them locked down in energy balance, but what we couldn't predict was this additional action of the microbes, which did lead to about a pound of weight loss in just an 8-day period on our diets. So the reason I would say, "Yes, this is ready for implementation," is because our diets align with current public health recommendations. It's already known that diets that are high in fiber and whole foods have benefit not just to weight loss

but also to overall health, so the great thing about our paradigm is that we had a variety of foods on our diets, meaning that people could take these four drivers—fiber, resistant starch, limiting processed foods, and eating larger whole foods—and they could implement that into what they typically eat every day that aligns with their culture, with their beliefs, and their preferences. So I would say, yes, this is something that could be implemented today.

Dr. Buse:
And as sort of a quick follow-up to that, how would you translate that into something for a person living at home? What is a resistant starch food? Is there a practical approach for people to do this at home?

Dr. Corbin:
Yes. So I love this question because I can put my dietitian hat on, which I don't get to wear very often. So if I was speaking to a patient, I'd say, "When you look at a food label, those calories on that food label are a really reasonable approximation of how much energy that food gives up when it's basically burned and how much of that is absorbed by us, but it doesn't account at all for the contribution of the gut microbes and the individual contributions of our personal gut microbes," because one thing that was very striking about what we found is that some people absorb 4 times more calories than other people on the Microbiome Enhancer Diet, so some people have much more robust effects of the gut microbiome. So because those calories on that label don't account for that, what we can do today based on our findings is make sure we feed the gut microbes. Eat more high- fiber foods like fruits, vegetables, and whole grains. Include foods with resistant starch like beans, seeds—like sesame seeds, for example—or potatoes that are cooled or pasta that's cooled because the cooling process actually increases the availability of resistant starch, and also limit as much as possible processed foods. By doing those things, and even if you eat the same amount of calories, you provide food to the microbes that will have benefits to you. So rather than thinking about restrictive diets, think about how you can upgrade your food choices.

Dr. Buse:
Wonderful. Is there anything else you'd like to add before we close, Dr. Corbin?

Dr. Corbin:
Yes. Just quickly I want to say again that obesity is a disease and weight management is hard. I'm a dietitian. I'm a nutrition scientist. And let me tell you, if somebody puts a cookie or ice cream in front of me, I'm going to eat it. I love those things. So it's not about how much you know. It's really about your mindset. And so I think this mindset of asking yourself every time you eat a meal or a snack "Have I fed my microbiome today?" could really be a practical way to improve your eating habits and improve not just your waistline but your health.

Dr. Buse:
Thank you for being here and for sharing your insights on diet and the gut microbiome.

Dr. Corbin:
My pleasure.

Dr. Buse:
For ReachMD, I'm Dr. John Buse. To access this episode and others from our series, visit ReachMD.com/Diabetes Discourse, where you can Be Part of the Knowledge. Thanks for listening.