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What to Know About the Microbiome & Probiotic Use

Dr. Buch:

Welcome to GI Insights on ReachMD. I'm your host Dr. Peter Buch. And joining me today to discuss what we need to know about the microbiome and probiotic use is returning guest Dr. Eamonn Quigley. Dr. Quigley is a David M. Underwood Chair of Medicine in Digestive Disorders, Chief of the Division of Gastroenterology and Hepatology, and Professor of Medicine at Weill Cornell Medical College at Houston Methodist Hospital.

Glad to have you back on the program, Dr. Quigley.

Dr. Quigley:

Great to be with you.

Dr. Buch:

Thank you. So, Dr. Quigley, let's begin with some definitions. What's the difference between microbiota and microbiome?

Dr. Quigley:

In the strictest terms, microbiota refers to the bacteria themselves, not just bacteria but fungi versus any other microbes that exist in a different environment. Microbiome refers to their genetic material. Now fortunately or unfortunately, these terms are often used interchangeably, and you'll even find experts referring to these terms interchangeably, so don't feel bad if you make this mistake. It's a common one. But strictly speaking, microbiota refers to organisms or microorganisms. Microbiome refers to genetic material.

Dr. Buch:

And let's just throw in another definition while we're in definitions: dysbiosis.

Dr. Quigley:

Dysbiosis is a term I don't like a lot because dysbiosis means, strictly speaking, that you've got a microbial population which in some way or other is abnormal. That, of course, assumes that you know what's normal, and that's a problem in many instances, including the human gut or other human organs, and so I tend to be a bit more vague and say that it's a disturbed microbiota or a microbiota that is different from control subjects. I think dysbiosis has been overused and has been used in situations where it's probably not applicable, but to get back to your question, dysbiosis refers to a microbiota which in some way or the other is deviated from normal.

Dr. Buch:

And you've got me thinking about a different perspective on this. I read once that the microbiome of North America is different from remote communities in the upper regions of the Amazon in South America. Do you want to comment a little bit about differences in microbiome?

Dr. Quigley:

Yes. So the study you're referring to is a very interesting one, and one that I refer to a lot when I'm giving talks. So this was a study that was done a few years ago now comparing the microbiome of individuals living in urban regions in the U.S., basically in major cities, to individuals who were living in two communities, and the Amazon basin actually in Venezuela and to rural Africans in Malawi, and what they found was that the diversity—and by diversity, I mean the number of different species in the gut microbiome—in individuals from either Africa or Venezuela was much higher than that of individuals in the U.S. Now the reason that's important is that, as a general statement, diversity is a good thing, and in general, in disease states, diversity tends to be reduced, and in health and in patients on healthy diets, diversity tends to be increased, so that was a very interesting finding.

Now the question is: what accounts for those differences? And I think the general feeling is that the major factor there is diet and that the rural, whether it's in Africa or those within the Amazon basin in Venezuela, were eating very much a plant-based diet whereas the individuals living in cities in the U.S. were eating a highly processed diet. And, of course, a plant-based diet is very positive for your microbiome whereas a highly processed diet is not.

Dr. Buch:

Yeah. The other thing that comes to mind with regard to that discussion is antibiotic exposure in these remote locations as opposed to the rest of the world.

Dr. Quigley:

Absolutely. So that's also emerged as a very important theme. We've known for a number of years that antibiotic exposure, particularly frequent antibiotic exposure in childhood and particularly in early childhood, seems to be a risk factor for the development of a number of conditions, from obesity to inflammatory bowel disease to irritable bowel syndrome later in life. Now of course, we believe that that is because of a disruption of the microbiome early in life. And now, why that's important has become clear in that for the first two to three years of your life, that's when your microbiome is developing, and after about three years, it reaches a plateau, and you really have your adult microbiome formed, and that remains fairly stable until later in life. So interventions or things that happen in those first few years in life can have a critical impact on the microbiome, but that impact may not be felt until later in life.

Dr. Buch:

Thank you very much. So if we zero in on the microbiome for just a few minutes, we talked about some of the factors that can affect it. We talked about antibiotics and food. What other factors can affect the microbiome?

Dr. Quigley:

So if you take any group of individuals in adult life, the big factors that affect the microbiome are age, diet, and antibiotics. Now the other big factor is that critical early period of life. There are a number of factors there which are influential: first of all, the way in which you were born. Are you born by vaginal delivery, or are you born by Caesarean section? That makes a difference. Eventually, you catch up, but in those initial few months or years, maybe couple years of life, it does make a difference. The second thing is how you were fed. Were you breastfed, or were you formula-fed? That also makes a difference. And then, what were you exposed to in your early period of life? Were you exposed to a lot of infections, or did you live in a very sterile environment?

And the other thing which I think you mustn't forget—and this becomes very important when we try to incriminate changes in the microbiome in disease states—is that diseases themselves can change the microbiome. So you may study the microbiome of a given disease and say, "Oh, it's all different," but in fact, that difference may be a consequence of the disease rather than the cause of the disease. But I think just to summarize, I think the main factors that influence the microbiome are birth mode, infant feeding, diet throughout life, antibiotic exposure, and then probably some other environmental factors that we're only beginning to understand.

Dr. Buch:

Thank you. Now, Dr. Quigley, what's the difference among probiotics, prebiotics, and symbiotics?

Dr. Quigley:

So a probiotic by definition means a live microorganism which, when ingested in adequate amounts, confers a health benefit to the host. A prebiotic is not an organism. It's a substrate, typically a carbohydrate, which promotes a healthy microbiome. If you combine a prebiotic and a probiotic, you've got a symbiotic. And there's a further term which has recently been introduced which is called a postbiotic. A postbiotic is a microorganism that has been attenuated but still retains some biological properties. It could also refer to components of a bacteria like its cell wall or some other components which has biologic activities. And there's quite a lot of interest in these postbiotics now because, of course, they don't have to be live. In fact, they're killed or attenuated so there aren't the same implications there are for storage or for storage in extreme temperatures, etc., so that's a term I think you're going to see more of in the years to come.

Dr. Buch:

Thanks for that. For those just tuning in, you're listening to GI Insights on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Eamonn Quigley about the microbiome and probiotic use in gastroenterology.

So, Dr. Quigley, let's now move on to some areas of controversy. Should we be giving probiotics to patients with irritable bowel syndrome?

Dr. Quigley:

Great question, and I will give you a somewhat complicated answer, and let me try to explain. So just to back up a little bit, irritable bowel syndrome is very common. It's a heterogeneous disorder. People have different symptoms, different severity of symptoms,

different frequency of symptoms, and undoubtedly, there's more than one cause of irritable bowel syndrome, but there are some hints out there that the microbiome may be relevant to irritable bowel syndrome, and let me just mention those.

First of all, there are a group of people who never had irritable bowel syndrome before but pick up salmonella, campylobacter infection, or food poisoning, and then develop irritable bowel syndrome, so-called post-infected irritable bowel syndrome. And secondly, there have been a number of studies which have shown that if you analyze the microbiome in patients with irritable bowel syndrome, in some it is different. Those findings are not consistent, but certainly, they do show that there are abnormalities. And then thirdly, there is data to suggest that certain antibiotics may actually help irritable bowel syndrome. And finally, there's also data, which I mentioned earlier, suggesting that antibiotic exposure may predispose you to irritable bowel syndrome. Now that's kind of a jumble of data, but what it says to me is that messing with your microbiome may play a role in irritable bowel syndrome.

Now to counteract that, there have been a variety of studies performed with probiotics, prebiotics, symbiotics, and with fecal microbiota transplantation in irritable bowel syndrome which have produced very good results depending on the strain that's used, depending on the dose that's used, etc.; but overall, for each of those therapies that I've mentioned that could modulate the microbiome, there is positive data. The problem is trying to sort it all out. So I would say in general, and I think many guidelines would agree with me, that probiotics are probably a useful therapy in irritable bowel syndrome, but which one to choose is a more difficult task because we don't have comparative studies, which is a problem.

Dr. Buch:

And along those same lines, should probiotics be used to prevent *C. difficile*?

Dr. Quigley:

There is good evidence that if you are taking antibiotic and if you're at risk for *C. difficile*—for example, if you're older—that a probiotic may play a role in reducing the risk of getting *C. difficile* or getting antibiotic-associated diarrhea in general. Don't forget that a lot of people get diarrhea with antibiotics that's not caused by *C. difficile*. It's just caused by their disturbance in the microbiome caused by the antibiotics. So, yes, I think that's a strategy that I encourage patients to do is that if they are taking antibiotic, and particularly if they have had *C. difficile* in the past, there's probably no harm to take a probiotic. And again, there is data suggesting that some probiotics in that instance may be better than others.

Dr. Buch:

And from your vantage point, Dr. Quigley, which probiotics are the best?

Dr. Quigley:

Well, I won't give you a straight answer to that question because I think it depends on the situation, it depends on the condition, and it depends on the patient population. For example, I mentioned in terms of *C. difficile* there's a probiotic which actually is a yeast called *saccharomyces boulardii* which has quite good evidence for prevention of *C. difficile*-related infection or for antibiotic-associated diarrhea or for preventing daycare diarrhea in children, for example. There are some lactobacilli that have good evidence for irritable bowel syndrome. Perhaps, bifidobacteria may have the better evidence. So it depends on the situation. It's like anything else; you wouldn't recommend one medication for everything.

Dr. Buch:

And before we conclude, are there any other thoughts you'd like to share with our audience today?

Dr. Quigley:

Yes. I think the microbiome area is amazing, and it's been one of the revolutions in medical science over the course of my career, and there's tremendous basic science. I think what's been more difficult to interpret and more difficult to do are studies in humans because there's such variation in the microbiome that you need very large studies. And I think there's been a bit of a rush to incriminate the microbiome as the cause of everything, and I think we need to be a little bit more cautious in interpreting these studies and, as I mentioned earlier, in separating cause from consequence. And similarly with probiotics, because they're not regulated the same way as drugs, many of the studies were small, maybe not optimally designed, and I think we need better studies in that area also.

Dr. Buch:

This was a great discussion on the microbiome and probiotics. I want to thank my guest, Dr. Eamonn Quigley, for this timely information. Dr. Quigley, it was a pleasure having you on the program.

Dr. Quigley:

Delighted to be with you.

Dr. Buch:

For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights where you can Be Part of the Knowledge. Thanks for listening and see you next time.