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2020 Crohn's & Colitis Congress: Research Takeaways

Announcer:
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Here's your host, Dr. Matt Birnholz.

Dr. Birnholz:
Coming to you from the 3rd Annual Crohn's and Colitis Congress in Austin, Texas. This is ReachMD. I am Dr. Matt Birnholz. Joining me to walk through some of the hottest bench-to-bedside research updates being discussed at this years' Congress is Dr. Maria Abreu, Professor of Medicine and Microbiology and Director of the Crohn's and Colitis Center at the University of Miami. Dr. Abreu, welcome.

Dr. Abreu:
Thank you.

Dr. Birnholz:
So just to start off, I will ask you the broad question first, sort of the million-dollar question, and that is: what research updates, in general, have garnered a lot of attention, or at least gotten on your radar, this year and at this Congress? Do they hover around a similar basic science category or are they across the board?

Dr. Abreu:
I mean, I am always turned on by the microbiome and all the implications of manipulating the microbiome in any number of ways to treat IBD in some direct ways and some indirect ways, like diet and all that. Yesterday, a colleague of mine, Dr. Johnathon Braun, who is now at Cedars-Sinai, extraordinarily accomplished scientist. He is a pathologist and actually had been head of pathology at UCLA and is now at Cedars-Sinai just down the street and we co-organized a session and it's his brain child really. You know, having to do in a way intercalating the brain and pain and the microbiome as it relates to IBD. So it's kind of a novel perspective, and we had, you know, senior people speaking on topics that we kind of knew what to expect and also we had, as you know, these sessions have also abstracts that were the highest rated abstracts. And the way it actually works behind the scenes is, we're given the highest rated abstracts and we're allowed to pick from those abstracts to decide which ones fit our session, right? So we picked ones, but we wouldn't have known what exactly that we're going to talk about. It was just a fantastic session because it fired on all cylinders. I almost feel the cure for IBD is knowable. If we could get all this brain power. You know, we talk about network, analysis, and all these things, but there is so much information. If someone were smart enough to put it all together we could kind of unlock some of the secrets. So in this session, you know, starting in no particular order, there are people who are still interested. I shouldn't say it that way, but who who study that lining of mucus that is, at least, one barrier to the penetration of bacteria and other things into the epithelium and into the gut, right? And you can imagine that if you've ever looked at a picture of what the endoscopy looks like and IBD, it looks like somebody is eating the tissue. It looks like there's an attack going on. And so it makes sense that if you've got a problem in that, in that fence and kind of that barrier created by mucus that could be problems and not surprisingly, you know, a particular investigator, who has been working on this for a while is using genetic models to mess up your mucin, mess up that lining, and showing that you can get spontaneous inflammation and it worsens cancer risk and all this sort of stuff. So I kind of think that there's that, I mentioned that because I think that if we're ever going to really do a better job of treating IBD, we've got to tackle all the different things that go awry. Even if it's only going to be taking care of one part of the story. You know, we focus a lot on the immune response, which most of the drugs that we use for the treatment of IBD are directed at that, and we need more drugs that are directed at making that picket fence stronger. There are a lots of great

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microbiome-related talks that were given in the session. One of them is from a young guy, Johnathon Jacobs at UCLA, who has a very interesting cohort. He's followed their patients with IBD, right that, and, you know, it's well known that people with IBD have an abnormal microbiome, right? But he also has healthy, unaffected relatives of those IBD patients. So that these are people that in theory are the higher risk of developing IBD, but they don't have it, right? Because one of the conundrums for us is the chicken and egg problem, the chicken and problem, which is to say that if once they have IBD the microbiome goes awry, and so, therefore, is it really that the microbiome is the initial problem or is it just a consequence of having inflammation, right? So he took these healthy first-degree relatives and divided them into two groups; those that had a microbiome that looked kind of like the IBD people, but they didn't have IBD and those that had a microbiome that was more like a healthy person. And if he used that microbiome of the, he called it like type one and type two microbiome, but the microbiome that looked like the IBD person, but they don't have IBD, and transferred it into germ-free mice, he could see that there was a beginnings of a problem in these mice that they were they were susceptible to developing inflammation. Again, suggesting that microbiome really can play, I don't want to say quite a causal role, but almost a simultaneous role in developing IBD and we focus a lot on bacteria. It became not quite trivial, but much less difficult to sequence bacteria, we usually use 16S sequencing and the cause has come way down like a lot of sequencing cause to describe like who's living in the gut in terms of, you know, molecularly. Although, we still have this big gap of doing functional studies of those bacteria. But what has been less studied are viruses and fungus, right? And so we also coexist with a lot of fungi and Iliyan Iliev, who's at Cornell, he, and then he had also a post-doc, spoke about how in IBD patients; actually, they also have dysbiotic fungi. It's not just only about bacteria. There is a disruption in normal fungi and less diversity in normal fungi. And he's gotten a hold of the samples collected from patients who were in a clinical trial of fecal microbial transplant for ulcerative colitis. There was a very, you know, this is not new news, but where these patients with UC got fecal transplants, they got better. Some didn't. Some did. And he is finding that at baseline, some of the people, who have the most abnormal fungi to start are the ones less likely to respond. So that maybe there are predictors in that world and that kingdom of who's going to respond and who's not going to respond.

Dr. Birnholz:
So not necessarily a smoking gun, per se, but, but maybe an important contributor that has been overlooked among others.

Dr. Abreu:
Yea.

Dr. Birnholz:
Fascinating.

Dr. Abreu:
You said it better than I did. Absolutely right. That that's been overlooked. A friend and colleague came from Israel, and she gave a talk on diet. That's always the Holy Grail. I probably would summarize her talk as saying we should all be on a Mediterranean diet and that maybe in the context of IBD, we could using microbiota analysis, some more personalized. Like, for you, you got to eat a lot of apples and for the other person, you got to eat a lot of nuts. That we could, you know, jump start it a little bit because just diet, at least for now, is an adjunct to the treatments that we use for IBD. There are two kind of neuro-related talks that I'm going to mention and then, then I'll shut up. One is that a colleague of mine at the University of Miami has very interesting data. And to some extent, in some of the pay samples that we've provided her, that opioids worsen IBD. So, most of her studies are using hydromorphone has the strongest effect, which is commercially known as Dilaudid. And in mouse models, if you give mice Dilaudid, you know hydromorphone, they get intestinal inflammation and they have translocation of bacteria and more permeability in their gut. And if you layer on a chemical that causes inflammation, these animals get very sick, so many of them die. And that's important because a lot of studies have shown that there's a higher rate of mortality in IBD patients on opioids, which we always ascribed to there are sicker, there are sicker patients and, therefore, ergo, they're going to die more often. But it could very well be the case that, in fact, it's actually worsening the disease and so the clinical implications of that are huge. The first thing that a patient flaring from their IBD gets is hydromorphone in the ER. So this is, I think, I often use it when I'm talking to patients about why we really need not to use narcotics as the way to treat IBD and I understand that they're suffering and I understand all that, but I think that this is why we're making them worse, or one of the things. And then the last thing I will tell you about a genius neurogastroenterology, as it relates mostly to irritable bowel syndrome and really trying to understand the biology of what's happening in the brain in patients with IBS is now applying a lot of that to IBD patients. And it has shown that if you do PET scanning, or functional MRIs on these patients with IBD, and I think he used ulcerative colitis as a cohort, their brain signaling is different. You know, there are parts of their brain that are much more active. Like a muscle that you've pumped up because of so much signaling and that there are certain phenotypes of people that, you know, have a lot of neuroses and there are ways to measure that. Actually to have a measure of how neurotic you are, and it sounds like we're saying that they are crazy, they are not. It's biology. It's, you know, how you react to stressors that actually have more frequent flares because of it. So I think that that's another huge thing. Every patient I see says "stress makes my disease worse," right? And we say, ah, that can't be, but it can be. We just never were

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intelligent enough to find that link. So I learned a lot. I don't think I can learn anymore at this meeting.

Dr. Birnholz:
What do you think is most instantly translatable into changing clinical practice paradigms? Certainly from your vantage point, you were looking at the potential effect that opiates can play in in worsening inflammation, saying "I need to start changing my recommendations fast." Were there any of these studies that, that were sort of jaw dropping for you, that made you say "Hah, we got to move in on this really quickly?"

Dr. Abreu:
Well, I think, you know, there is a difference between something that really seems amazing and the things that are more quickly actionable. And the more quickly actionable, of course, you know, avoidance of opioids, it would be one, but I think the other thing that we could be doing immediately is at least in the IBS world, there is some reversibility of those brain patterns when you have cognitive behavioral, you know, therapy for these patients, and I think that we offer it in our in our clinic, but, you know, for most gastroenterologists, it is very difficult to. They need to set up ways to send people to therapists, to send people to psychiatrists because I suspect that getting their anxiety better will also help deter flares. I also think people, many patients, every patient wants to know what they should eat, but not many patients want to change their behavior even when you tell them that, what they should eat and not to mention that so many doctors will say "Oh, you know, you can eat whatever you want." I hear that still from my patients that they could eat whatever they want, and they can't. You know, as far as I am concerned, I don't want to throw away all these very expensive, you know, biologics if the person isn't going to kind of meet us half way and try to do something to compliment that by having some control over their diet, right? We just finished a study that we've submitted for publication, but within ulcerative colitis patients we did a diet intervention study, but what I wanted to say to you is, at baseline, people were eating crap, absolute crap, like there was almost no consumption of fruits and vegetables at baseline.

Dr. Birnholz:
So, standard American diet.

Dr. Abreu:
It was a standard American diet and actually we had two groups, we had a low-fat diet group and we had, what we called, a standard American diet group. We had to revise that and call it an idealized standard American diet because it was so much healthier than what everyone was eating at baseline, or what most people were eating at baseline. So, we have a long way to go. Again, even when patients tell you, oh they want to change their diet, they don't because it's hard.

Dr. Birnholz:
It makes it particularly daunting, in that area. Where do you think the buck stops for the specialist in IBD versus other members of a multispecialty group to be able to really take the reins on helping patients through issues such as that?

Dr. Abreu:
Well, we're not paid for talking to patients like we should be, right? And things like dieticians and psychologist are not easily paid for. And so, it's not entirely; as you said, it takes a village actually to take the best care of IBD patients. I think that for clinicians, they could make a virtual village. Try to identify someone that is a dietician in their community that has some knowledge, because again there are so many quacks in every field. Someone who can deal with cognitive behavioral therapy for stress for a lot of these patients. That's kind of like low lying fruit for these people, because our time is taken up by fighting with insurance to get approval for drugs and dwindled away from what really matters most, which is getting people better. So, it does take a village, and I think that in all of our villages, we need to have good dietary support. We are working on ways to try to deliver that by Skype, so that we can try to fill that gap.

Dr. Birnholz:
You're in a unique position as an expert in both bench research level and the clinical research level and the clinical care level, so triple threat. You have a great vantage point on seeing bench research catapulting over to clinical outcomes changes and change in the paradigms of how we care, but let's flip it around. As somebody who sits in all those chairs, how are the clinicians and the input coming from the experts in the field at this Congress, feeding back on being able to improve the bench research for the basic scientists here?

Dr. Abreu:
I think that's huge. I mean I feel that's a niche for this Crohn's and Colitis Congress, is to have more intimacy and have basic researchers come and hear what the clinical challenges are. We certainly have a lot of them. I mean, there is just a lot to work on. And it makes me so excited to see like young people excited about the field, and you know, yesterday I went through the poster session. There was a lot of energy there, and that's what we need. I am always humbled when I give talks to graduate students or to medical students, that they have like the best questions because they ask very fundamental questions that you've kind of thought, oh, never

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thought about that. And so we need more people like that to have those ah-ha moments, and I think they're here learning what the challenges are, like all the gaps we have in our care, all the shortcomings of the drugs that we currently have, so I hope that they've learned by osmosis at this meeting.

Dr. Birnholz:
Well, I very much want to thank my guest, Dr. Maria Abreu, for joining us to talk about some of the key takeaways from the bench and clinical research arenas. Dr. Abreu, it was fantastic talking with you. Thanks again.

Dr. Abreu:
Thank you, Matt.

Dr. Birnholz:
For ReachMD, I'm Dr. Matt Birnholz. Thanks for joining us everyone.

Announcer:
This program was brought to you in collaboration with the Crohn's & Colitis Foundation & the American Gastroenterological Association. If you missed any part of this discussion, or to find others in this series, visit ReachMD.com/foundation, where you can be part of the knowledge.

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