Probiotics & Dysbiosis

Featuring:

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Adam Baker, MD, Director of Science, Human Health Innovation, Christian Hansen
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TRANSCRIPT

Maura Bowen: Hello listeners. I'm going to kick off today's *Power of Nutrition Podcast* episode with a story about a tiny fighter. His name is Grayson. He was born at 27 weeks' gestation weighing only about 1,000 grams because his mother had severe preeclampsia and her obstetrician recommended delivering by caesarean section because it just wasn't safe for Grayson to stay in utero much longer. And he did really well for the first few weeks of life, easily weaning to C-PAP and taking in fortified breast milk. But soon, he started to struggle with tolerating enteral feedings. So given his history, his NICU team monitored him for signs of necrotizing enterocolitis. And as you know, NEC is a devastating disease that affects most pre-term infants that can progress very rapidly. Grayson had many of the risk factors related to intestinal dysbiosis, having been born pre-term and delivered by caesarean, exposed early to antibiotics, and with poor uterine environment.

His care team knew strengthening his gut microbiome would be a critical part of his nutrition therapy so he could better tolerate his enteral nutrition. NICU nurses, dietitians, physicians, you probably know this story by heart. The microbiome plays such a critical role in the well-being of our smallest patients, and sometimes it takes every tool available to help ensure pre-term newborns get stronger and thrive.

I'm Maura Bowen with Abbott Nutrition Health Institute, and I've invited two *Power of Nutrition Podcast* regulars, Dr. Karen Wulf, who is Abbott Medical Director and practicing pediatrician, and Dr. Adam Baker, Director of Science, Human Health Innovation from Christian Hansen and Herschel in Denmark to today's discussion. And we're also honored to host Dr. Arpitha Chiruvolu, a practicing neonatologist who is joining us from Baylor University Medical Center in Dallas, Texas. All three doctors have dialed in not just for this recording, but for another podcast focusing on probiotics and practical use in the NICU. So be sure to listen to that recording. And in the meantime today, we'll focus on the role probiotics can play in helping to establish a healthier microbiome and improve outcomes for pre-term infants. Welcome doctors.

Dr Wulf: Thank you, Maura. Happy to be here again.

Dr Baker: Thank you Maura. Also very happy to be here again.

Dr Chiruvolu: Thank you Maura for the invitation. I'm excited to participate in this important podcast.

Maura Bowen: So let's give you each the opportunity to introduce yourselves. Dr. Chiruvolu, since you're new to this podcast, would you like to go first?

Dr Chiruvolu: Thank you, Maura. I'm a neonatologist in practice for over 15 years currently working at Baylor University Medical Center in Dallas, Texas. I also serve as an assistant professor of pediatrics at Texas A&M College of Medicine. I'm a clinical researcher in the field of neonatal perinatal medicine.

Maura Bowen: Wonderful. Thank you for that. Now, Dr. Baker, would you like to go next?

Dr Baker: Thank you, Maura. Yes. So I'm a human medical geneticist who spent most of my career studying complex diseases and oncology. But for the last 10 years I've been working at Christian Hansen as the Director of Science, where I've been studying the microbiome and in particular how probiotic bacteria can work and affect and support human health.

Maura Bowen: Wonderful. And Dr. Wulf, can you tell us about your background?

Dr Wulf: Sure. I am a general pediatrician and I've been in practice over 18 years, and I joined Abbott almost three years ago as the Medical Director for Pediatrics.

Maura Bowen: Wonderful. Now, before we start, I should note that I'm recording in the studio while Dr. Wulf, Dr. Baker and Dr. Chiruvolu are dialing in from their respective offices. So you may notice some tonality differences across this recording. And I'll also note that Dr. Wulf will conduct today's interview and provide her insights alongside Dr. Chiruvolu's and Dr. Baker's answers. Dr. Wulf, the microphone is yours.

Dr Wulf: Thank you so much, Maura. So let's start from the beginning. Dr. Chiruvolu, what happens to the gut microbiome when an infant is born?

Dr Chiruvolu: When an infant is born, the gut does not have many bacteria. There is low bacterial diversity. With time as the gut matures, the microbiome composition changes and the diversity increases. In fact, the infant gut microbiome changes radically from birth to one month of age.

Dr Wulf: And how is this different for a pre-term infant in the neonatal intensive care unit setting?

Dr Chiruvolu: The normal intestinal flora differs greatly between a pre-term and a term infant. pre-term gut microbiome is less diverse than term microbiome. Pre-term intestinal barrier is also immature and permeable to potential harmful bacteria compared to term infants. Pre-term infants in the NICU may also get exposed to antibiotics and other drugs that may adversely influence the microbiome.

Dr Wulf: So knowing this, what are some of the major health challenges that pre-term infants might face focusing more specifically on the gut microbiome?

Dr Chiruvolu: Significant proportion of neonatal sepsis is actually with gut-derived organisms, suggesting gut as one of the main origin for infection. Dysbiosis also increases the susceptibility to necrotizing enterocolitis. NEC is a multifactorial process of intestinal infection and inflammation involving abnormal bacterial growth.

Dr Wulf: So you mentioned dysbiosis. What is it and how do you recognize this in a pre-term infant?

Dr Chiruvolu: Dysbiosis refers to abnormal alteration of microbial composition. Fecal samples of infants are helpful in detecting dysbiosis. Infants with necrotizing enterocolitis had fecal samples with abundant harmful proteobacteria, sparse, beneficial Bifidobacterium, and less diversity.

Dr Wulf: That's really interesting. So, Dr. Chiruvolu, are there nutritional interventions that might help improve dysbiosis in these infants?

Dr Chiruvolu: Introduction of healthy probiotic bacteria may suppress harmful bacteria and increase diversity. There is abundance of data supporting this biological plausibility with consistent benefits and minimal risk. Administration of mother's own milk also improves dysbiosis. Multiple components of human milk protect against sepsis and necrotizing enterocolitis. Oligosaccharides are complex carbohydrates produced in human milk, which serve as energy source for the good probiotic bacteria.

Dr Wulf: So you've given us some interesting information about the gut microbiome in the pre-term setting and suggested about probiotics that this might be a helpful intervention. Why do you think probiotics administration in the NICU has not been widely adopted yet in the US?

Dr Chiruvolu: So Dr. Wulf, although there is abundance of research supporting probiotic use in pre-term infants, there is still uncertainty regarding strain and dose due to wide variation in clinical trials. There is also a potential for probiotic associated sepsis, although reports of which have been very limited. There is paucity of long-term follow-up studies, although two studies reporting outcomes did not show any adverse effects with probiotics. And above all, probiotics are considered dietary supplements with no FDA approved probiotic drug formulation currently available in United States.

Dr Wulf: That's really interesting. Dr. Baker, I'm going to turn this over to you for a moment. Could you speak to quality and safety and the manufacturing process for probiotic use in the NICU?

Dr Baker: Yes. Thank you, Dr. Wulf. I think it's critically important. And as you heard in the last comments, we have to consider safety; we have to consider the quality and what we're actually giving to these very, very vulnerable infants. So let me talk about... You asked about the manufacturing process, particularly ISO seven. We start to think about food safety and hygiene monitoring, and you have to consider at the highest level when we're dealing with such critical cases in such vulnerable infants. So the ISO seven is where we start to do monitoring, and we're actually monitoring all processes involved in the manufacturing process.

We actually are monitoring as we grow the bacteria and then during the sort of purification and getting the bacteria ready for the product. What you're actually doing is monitoring the environment, monitoring the product mixing the raw ingredients go into the product, and making sure every one of those stages is critically tested positive [inaudible 00:08:10] environmental considerations in place, if you're going to use that product in that age, in those bacteria. And this is one of the highest levels you can do in the food supplement space. And I think that's what we need to think about, it's particularly what we need to think about in these areas.

Dr Wulf: Thank you, Dr. Baker. I have another question for you. Could you talk a little bit about the benefits of a multi-strain probiotic versus a single-strain and why this might be important consideration in the pre-term infant space?

Dr Baker: Yes. We're learning about the probiotic bacteria that one strain can have some beneficial effects, but we can have bacteria that have different types of beneficial effects. And we do know that not just one bacteria is what makes up a healthy microbiome. We're looking for that sort of increase in diversity. So if we have the opportunity and we can actually compliment one, two, three strains with complimentary efficacies--demonstrated effects, then in this case more can be better because more is actually building up what we want. We want to build up the diversity of the microbiome and that's what we're looking for.

Dr Wulf: So we're constantly surveying the literature I want to bring to our audience, current opinions and what's going out there. And I recently read an opinion piece published by the American Medical Association on the JAMApediatrics.com website. And it was discussing some uncertainty around using probiotics to reduce necrotizing enterocolitis. So the article suggested that practitioners have two reasonable options when deciding to use probiotics for this purpose. Either one, wait for results of ongoing trials, or two, accept the current body of evidence that suggests the benefits of probiotics used in this population outweigh its potential drawbacks. Dr. Baker, first I'd love to get your thoughts and then Dr. Chiruvolu.

Dr Baker: Well, I think, yes, we're noticing there's many, many babies have been treated with probiotic bacteria and we've seen the effects in the clinic. But sometimes there is a concern when we use the word probiotics and we're generalizing, I would say. But not all probiotics are the same and we need to carefully consider which probiotic strains, which probiotic product are we actually using? And then I think you would

actually start to see that maybe there is stronger evidence of certain bacterial strains than others. And this is the type of approach we need to start to consider. We need to know which probiotic strains are being used, how they're being used in the dose, and then we can start to build up this very good clinical evidence. And there is very, very good evidence for the three strains of bacterial probiotics, but they've actually been used and demonstrated that they actually reduce the risk of NEC by 50%. And so when we start to look at these types of approaches, we can look at that evidence and see this particular set of strains worked clinically, and we start to build up that evidence.

Dr Chiruvolu: With over 50 randomized control trials, 30 observational studies, and 80,000 infants studied, there is clear evidence that probiotics are beneficial in pre-term populations. In my opinion, additional studies are not really going to change this. I concur with the published viewpoint that the units considering probiotic implementation may do so with evidence-based guideline and good surveillance in place.

Dr Wulf: Well, thank you both. I agree. I think evidence-based practice is important and I appreciate both of your summarization of the current evidence.

Maura Bowen: Fantastic insights, as usual. I'd like to thank all three of you for sharing your thoughts on probiotics and how they can be beneficial for pre-term patients with NEC and dysbiosis. And it goes without saying, you all are welcome on the ANHI Power of Nutrition Podcast anytime. And of course, Dr. Chiruvolu, you and Dr. Wulf and Dr. Baker will be back again for our next episode, which focuses on probiotics and practical use in the NICU, so I'm very much looking forward to that conversation.

Dr Wulf: Thanks so much, Maura.

Dr Baker: Thank you very much, Maura.

Dr Chiruvolu: Thank you, Maura. Looking forward to the next episode.

Maura Bowen: For our listeners, if you're looking for more podcasts, we have dozens and dozens across a variety of different nutrition science topics, and you can find them on ANHI.org by clicking *Resources* at the top of the page, then *Podcasts and Videos*. We're also on Spotify now, so be sure to subscribe to ANHI's *Power of Nutrition Podcast* series to hear the latest nutrition science news and share us with your colleagues. And be sure also to visit Christian Hanson's The Probiotics Institute, that's ThePrebioticsInstitute.com to learn more about how probiotic strains can benefit the microbiome across the life cycle. The Christian Hansen team just launched a new global site as well as a site just for its audience in China, so visiting the site will be solid time spent. Thanks everyone.