

THE ROLE OF HUMAN MILK & HMOS

IN NUTRITION, NEONATAL DEVELOPMENT AND IMMUNITY

Featuring :: Lars Bode, PhD

TRANSCRIPT

Maura: Human milk is really fascinating, isn't it? Often, it's the first thing we feed our babies, and it boasts all the essential, nourishing elements they need, like water, fat, carbohydrates and protein. Just as importantly, within this mix is this ingredient that is strangely indigestible—a class of sugar molecules called human milk oligosaccharides—HMOs—which exist not specifically to *feed* baby, but to bolster healthy gut bacteria, assist in cognitive development, and help in a host of other ways.

Maura: HMOs were discovered in the 1930s. But it wasn't until recently that researchers have come to understand why they exist and the role they play in neonatal growth and development.

Maura: I'm Maura Bowen, and I'm podcasting for Abbott Nutrition Health Institute. We've invited today's guest—Dr Lars Bode (PhD)—to talk about the latest research on the components of human milk, focusing on HMOs and the role they play in neonatal nutrition, immunity, growth and development.

Maura: Dr Bode is a professor of Pediatrics in Neonatology, Gastroenterology, Hepatology and Nutrition. He's the Larsson-Rosenquist Chair of Collaborative Human Milk Research, and Director of the Larsson-Rosenquist Foundation Mother-Milk-Infant Center of Research Excellence at the University of California, San Diego, here in the United States. In other words, he's a busy guy, and we're lucky to have him join us today.

Maura: Hello, Dr Bode, and welcome!

Dr Bode: Hello! Thank you for having me and thank you for inviting me to speak at this podcast about human milk in general and human milk oligosaccharides in particular.

Maura: We're so glad you're here. There's one thing I'd like to note for our listeners: This podcast recording may sound a little different than you're used to hearing; that's because I'm still practicing social distancing from my work office in Columbus, Ohio, and Dr Bode is dialing in from the great state of California.

Maura: So Dr Bode, before we start, can you tell us a little bit about yourself, your current role, and what brought you to this area of focus in your career?

Dr Bode: Yeah, thank you. You've introduced my different roles and the different hats I'm wearing nicely already. My lab here at UC San Diego, that is specifically dedicated to research on human milk oligosaccharides, trying to understand what they are, how they're made, and what their benefits are for infants. During that research, which is now 11 years ago that I started, we noticed that there's more than just human milk oligosaccharides in human milk. Human milk oligosaccharides have an affect on so many different things, so many different tissues, so many different organs and health aspects, and we're certainly not experts on all of these. So, we realized we really needed to broaden our collaboration and find people who have this expertise. So, in the past we've really done this more by coincidence—we were running into people at conferences, or friends and colleagues. And at one point we said,

“let’s formalize that. Let’s formalize how we initiate these collaborations, and that’s really how we started our Mother Milk Infant Center of Research Excellence that I’m directing. There, we’re not just looking at human milk when it comes to infant health, we’re also looking at maternal health. For example, we know that moms who breastfeed have a lower risk of breast and ovarian cancer or cardiovascular diseases. But we’re also trying to learn from human milk to see what components are in human milk that we can potentially develop into new therapeutics for people of all ages—whether that’s chronic diseases or acute infections, we really want to know how we can leverage the power of human milk for people of all ages.

Maura: You are, of course, a leading expert on Human Milk Oligosaccharides. Can you share with us what you wish health care professionals understood about human milk?

Dr Bode: First, I think it’s wrong to detach human milk from the process of breastfeeding itself. Breastfeeding is more than just a delivery of ingredients. It’s really an intricate interaction between the mom and the baby. It’s not just molecules that are handed off to the baby for the baby to grow; there are so many other benefits to the process of breastfeeding.

Dr Bode: Then, I think it’s important to say that human milk is not just a mixture of molecules. It does change over time quite a bit. It’s really a dynamic tissue of complex molecules and cells that are different from mom to mom. It changes over the course of lactation. So I think it’s really important to understand that when we talk about human milk, it’s not just a list of ingredients.

Maura: You’ve touched a little bit already on the mother-milk-infant triad. Can you explain the triad a little bit more and also why it’s so important?

Dr Bode: Instead of just looking at human milk as the liquid we have with ingredients, it’s really important to understand the entire concept of mom, milk and infant. Whatever mom experiences is impacting human milk composition; human milk composition is impacting infant health; but it’s not just that linear. Also, whatever the infant is experiencing might impact human milk composition, so it’s retrograde feedback as well. The full triad is embedded into the environment. So, for example, if mom experiences certain pathogens in her environment and changes milk composition accordingly, then the changed milk composition hands over protective factors to the infant, and protects the infant from the different pathogens and the environmental factors mom experiences.

Maura: What makes human milk a *living* substance? Can you explain how it works?

Dr Bode: It’s really for two different reasons. One, it’s living because it’s dynamic; in other words, it changes composition over time and it responds to needs or environmental factors. But it’s also literally a living substance because it contains living cells. It contains immune cells that come from the mom. Potentially, there are stem-cell like cells in human milk. And then there’s also the recently-discovered mom’s-own-milk microbiome—so there are microbes that live in human milk. We always thought that milk is sterile, and that if not, then there must be some pathogens in there that cause disease. But really, we now understand there’s a microbial community that lives in human milk that is potentially beneficial.

Dr Bode: And really, the relevance of all this is really poorly understood at this point. We don’t know what each individual component does, but we also don’t really know how the different components interact with each other.

Maura: Your research has taught us that HMOs can impact infant health outcomes. Can you elaborate on some of the recent research for each outcome?

Dr Bode: There are different outcomes we can study both in the infant as well as in mom, but also short term and long term. I think we have to understand that HMOs are a group of 150 different components, different molecules, and each of these molecules can potentially have different effects on infants and moms. I think it’s important to

understand it's not just one HMO, it's a class of molecules.

Dr Bode: We've looked at growth and body composition; we have some data that oligosaccharides can potentially impact the risk for allergies; and in the preterm infant space, we found there are oligosaccharides that potentially protect from necrotizing enterocolitis or sepsis. So, looking at all this, I think it's important to understand that for some molecules, some of the effects that we see are microbiome dependent—these oligosaccharides shape microbial communities in the infant gut—and that has an effect on the infant. And we also know there **are** microbiome-independent effects—oligosaccharides directly interact with infant tissues either in the intestines or on a systemic level because these oligosaccharides get absorbed and reach the systemic circulation.

Dr Bode: So if we start with inflammation, we can look at acute inflammation, we can look at chronic inflammation, and there's evidence that specific oligosaccharides may have an effect on both. And again the effect might be mediated through the microbiome, but it might also be mediated by specific interactions with individual oligosaccharides

Maura: Can you tell us more about immunity as an outcome?

Dr Bode: We talk a lot about oligosaccharides shaping microbial communities, and then many times we talk about prebiotic effects of oligosaccharides, so meaning it shapes or helps develop microbes that can utilize human milk oligosaccharides and their metabolism. But we also see that specific oligosaccharides can protect us from certain pathogens. Individual oligosaccharides either stop the growth of some of these pathogens, or do not allow them to attach to surfaces and interact with immune cells that way. Or human milk oligosaccharides interact with immune cells and then booster the effect against these pathogens. So there are multiple different ways how individual oligosaccharides can impact immunity.

Maura: And cognition?

Dr Bode: That's a very interesting topic. We all want our infants to be smarter and our kids to be smarter. And there's some good data that looks at specific human milk oligosaccharides that contain sialic acid, and those oligosaccharides might contribute to brain development during the breastfeeding period. There's recent data that shows that specific oligosaccharides like 2'-fucosylactose—2'FL—in rodent models have an effect on learning and memory later in life, and we have just recently published a paper together with our colleagues at the Children's Hospital Los Angeles, where we found in a cohort study a strong association between the concentration of 2'-fucosylactose in breastmilk at one month of age and cognitive development at 24 months of age. So what happens in the very early stages, in the first few months of life and what oligosaccharides are present there seems to determine cognitive development later in life, which I find striking.

Maura: What about growth in this context?

Dr Bode: I think growth is something we have to view from two different perspectives. One, we talk about growth—when we talk about developed countries—we want to make sure our kids are not obese and develop associated diseases, so we're looking at whether there's anything in human milk that can prevent childhood obesity. And on the other side, in developing countries, we find oligosaccharides that are potentially associated with preventing malnutrition.

Maura: Is there anything a mom can do to change her HMO profile?

Dr Bode: That's a great question. Unfortunately right now we don't have enough evidence to make any recommendations what mom can do to change her oligosaccharides composition. I don't even want to say "improve" because we don't really know where to "improve" it to. We don't really know what is the optimal oligosaccharide profile for a mom and for a given baby, which really brings it back to the mother-milk-infant triad. So it

likely depends on all parts of the triad, what's optimal.

Maura: So with all that said, what do you think is in the future for human milk oligosaccharide researchers like yourself?

Dr Bode: I think the future is very exciting. It looks very bright. You mentioned that oligosaccharides had been discovered in the 1930s. I still think we're still in the very beginning of what all these oligosaccharides do. There are 150 different oligosaccharides, and we're looking at all these different outcomes, from growth and body composition to allergies to inflammation to infectious diseases, so it's really a wide spectrum of disease outcomes that we looked at and health outcomes. And one thing I'm really excited about is the long-term outcomes on bone health, on metabolism. We find, for example, that oligosaccharides early in life might reduce the risk of cardiovascular disease—so that's your heart attack and stroke – later in life. And again, is it possible that we can learn from anything we've seen now and the use human milk oligosaccharides and apply and use it for people of all ages.

Maura: One last question for you as a researcher: What do you think is important for practicing clinicians to understand about human milk oligosaccharide or human milk in general?

Dr Bode: One thing I would highlight is that having one oligosaccharide is not the same and will not do the same as the remaining 149 oligosaccharides. I think that's important to understand. And in the end, human milk is more than just the synthesis of individual oligosaccharides. The process of breast feeding is more than just human milk. And the last thought is that it's great that we have all this research, but breastfeeding and breastmilk should be the #1 choice for our infants.

Maura: This was excellent information, Dr Bode. Thanks so much for taking the time to record with us today. We appreciate all you're doing to help build awareness for HMOs and the role they play in nutrition and healthy growth and development.

Maura: Now, for our listeners, if you're hoping for more podcast episodes on nutrition and immunity, rest assured we're developing a series of additional episodes to help support you. You can find these recordings on anhi.org by clicking "RESOURCES" then "PODCASTS & VIDEOS." Don't miss an episode: Become an anhi.org member today by clicking "REGISTER" at the top of our homepage to receive regular nutrition science news updates from our team. Or, follow the Abbott Nutrition Health Institute on LinkedIn.

Maura: Finally, our website, anhi.org, has a series of printable resources related to this topic. You can find these resources on anhi.org by clicking "RESOURCES" and "PRINTABLE MATERIALS."

Maura: Thanks everyone. Stay healthy and safe.