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Immunity and Digestive Function in Infant Nutrition: Aiming to Thrive-Hot Topics in Infant Nutrition

Aiming to Thrive: Hot Topics in Infant Nutrition—Immunity and Digestive Function

Announcer Program Open

Welcome to CME on ReachMD. This segment, “Aiming to Thrive: Hot Topics in Infant Nutrition—Immunity and Digestive Function”, is sponsored by Prova Education and supported by an educational grant from Abbott Nutrition.

Your experts joining us today are Lars Bode, PhD, President, International Society for Research in Human Milk and Lactation (ISRHML) Associate Professor of Pediatrics Division of Neonatology and Division of Gastroenterology and Nutrition at the University of California, San Diego in La Jolla, CA; Sharon Groh-Wargo PhD, RD, Professor Pediatrics and Nutrition at Case Western Reserve University MetroHealth Medical Center in Cleveland, OH; and Terry S. Johnson, APN, NNP-BC, CLEC MN Neonatal Nurse Practitioner and Founder of Lode Star Enterprises, Inc. in Downers Grove, IL.

Dr. Groh-Wargo:

Hello, I'm Sharon Groh-Wargo. I'm a registered dietitian and neonatal nutritionist at MetroHealth Medical Center in Cleveland, Ohio. I'm also a Professor of Pediatrics and Nutrition at Case Western Reserve University School of Medicine and have spent my career providing clinical nutrition services to preterm and high-risk newborns. I'm glad to be here.

Dr. Bode:

Hello, my name is Lars Bode. I am the current President of the International Society for Research in Human Milk and Lactation, and I'm also an Associate Professor of Pediatrics here at the University of California-San Diego. My lab is dedicated to elucidating biosynthesis and functions of human milk oligosaccharides. And I'm also the Director of the UC San Diego MoMI CoRE, the New Mother Milk Infant Center of Research Excellence.

Ms. Johnson:

Sharon and Lars, thank you so much for joining me today for this very important discussion. My name is Terry Johnson. I'm a neonatal nurse practitioner with over 35 years experience in the intensive care nursery. I am a certified lactation education consultant, and I'm an Associate in the Society of Professionals for Patient Safety. My interests have extended into the human biology of human milk as well as nutrition in the NICU for the small preterm infant.

So, if I may, let me begin the discussion with some comments about immune functions that occur in the newborn infant's gut and how

they are linked to growth and health of the infant. When we think of the gut as an immune system organ, we have to realize it is the largest surface area that exists between the outside world and the inside world of the infant himself, and that the system has now been redefined as something we call a mucosal immunologic system, and this mucosal immunologic system exists in three parts primarily. One is going to be the pulmonary bed. The second, and the largest, is going to be the gastrointestinal tract. And the third is going to be the genitourinary tract. All of these areas uniquely interact together as they interact with microorganisms in the outside environment and the baby's own emerging competency in his immune system function. They are not separate but actually very well integrated by tissue, by immune cells, and by signaling molecules that move from one system to the other as the baby is encountering his first contact with the outside world.

The lining of the gut itself makes up the largest immune system organ that we have, the GI tract, second being the pulmonary bed, third genitourinary, and finally, the skin, all places where the baby's immune system must interact with threats that might come from the outside world. And at no time in his life is it more important than immediately after birth. So, let's begin the discussion with the immune functions that occur in the newborn infant's gut and how they are linked to growth and health of the infant.

So, Sharon, we often hear about human milk proteins, fats, and the milk sugar lactose, but what are the functions of the bioactive components in milk, including human milk oligosaccharides, or HMOs?

Dr. Groh-Wargo:

Well, Terry, that's a great question. As a nutritionist, I've traditionally thought of human milk as a feeding, but what has become abundantly clear more recently is all of the sort of nonnutritional factors, if you will, and human oligosaccharides are a huge portion of that. Human milk oligosaccharides are basically anti-inflammatory and antimicrobial constituents of human milk, but they have just a wide range of functions including functions as prebiotics, as antiadhesives, antimicrobials. They directly affect intestinal function and lymphocyte function and help to feed the brain, if you will, and each one of these functions has been explored in a lot of detail, so human milk oligosaccharides are a huge portion of the protection that human milk offers babies.

Ms. Johnson:

It's interesting what you said, Sharon, because we know a lot about oligosaccharides as they appear in human milk and even in colostrum and how it's unique how nature has provided these for the baby as he comes out as first feeding. These are made and made available to him early in colostrum and then later in mature and transitional milk, and they provide for him these immune properties that help him as his immune system continues to develop outside of the protective environment of being in utero as he comes in contact with more and more microorganisms. I think it's interesting that nature has made them extremely abundant in human milk, both in types and numbers, and that there's even more in our preterm population, who are the most vulnerable of infants. And there's diversification across women and across populations in the kind of HMOs they make, and all of those speak to the, I think, essential role that they play in the development of the immune system, not just as a nutritional element but as part of the baby's basic immunity.

And, Lars, please?

Dr. Bode:

I was going to just emphasize what you said before and just reiterate that it's a highly fascinating field, oligosaccharides in human milk highly understudied, although, they are the third most abundant component in human milk after lactose, the typical milk sugar, and lipids, fats. So, we have these human milk oligosaccharides, and human milk is very unique when it comes to the oligosaccharides. Bovine milk hardly contains any oligosaccharides, and being the basis of most infant formula, there's hardly any human milk oligosaccharides in infant formula today. And with the oligosaccharides having such profound effects on the infant's gut microbiome, the immune system either directly or indirectly, there's a huge difference at this point whether we feed an infant with breast milk or with infant formula.

Dr. Groh-Wargo:

You know, Lars, that's so interesting. I found recently sort of quantification of the amount of oligosaccharides in colostrum versus mature milk, and babies don't get a lot of volume of colostrum, but the concentration of the oligosaccharides in colostrum, it's amazing,

so it really is so important for babies to get that early milk because it really does provide them with a lot of protection. I mean, the oligosaccharides continue, certainly, in mature milk, but the concentration in colostrum is pretty impressive.

Dr. Groh-Wargo:

It also is particularly important in the neonatal intensive care unit. I mean, all babies deserve protection, but many of us have worked with that preterm population, hospitalized newborn population, and it is really important for them to be able to take advantage of that very special protection.

Ms. Johnson:

I think it's interesting. Joseph Nu has spoken of the concept of immunonutrition, the idea that not only are we feeding for basic nutrition for weight gain, for appropriate growth, but that in human milk with these human oligosaccharides and the other immune factors that are found in it, we have the opportunity to provide immunonutrition to these infants, not just nutrition in and of itself, but further development, elaboration, development of their immune system function that goes throughout their lifespan in providing a better state of health for them, as we saw in the AAP's metaanalysis of infants who were human milk fed.

Lars, how many different HMOs are there in human milk, and what are their range of functions?

Dr. Bode:

So, we have about 150 different oligosaccharides annotated and described so far. There might be many more. Some people talk about 200, 300 different oligosaccharides, so no, the exact structures are not determined yet. And the question then is: Why do we have so many different oligosaccharides and in such high abundance? What do they do? What's the benefit for the infant, potentially for the mother? And there's multiple facts. We always think of human milk oligosaccharides as being the prebiotics of human milk that shape the microbiome composition early on in life, so what kind of microbes can thrive and develop on these oligosaccharides, use it as metabolic substrate and build a foundation of the microbiome in the infant's gut. But there's really more to it. There's direct effect on certain microbes, that they have antimicrobial effects and just prevent certain microbes from growing or even kill them. There is effect as antiadhesive, so some of the bacteria, some of the pathogens need to attach to the epithelial cells in the infant's gut, and the oligosaccharides have been shown to mimic some of those adhesion factors on the epithelial cells and they prevent blocking of certain pathogens to the epithelial lining by serving as antiadhesive structure analogues. So, that's direct effects in the post microbe interface in the gut, potentially also in the respiratory system. And very important to highlight, about 1% of the oligosaccharides gets absorbed intact, makes it into systemic circulation, can have an effect on organs beyond the GI tract, and is excreted intact with the urine, so potentially also effects on urinary tract infections, brain development, many, many other things that we can think of, and we probably have only touched the tip of the iceberg when it comes to defining the effects of these different oligosaccharides.

Ms. Johnson:

Lars, am I correct in that these human oligosaccharides are not only protective against bacteria but other types of organisms as well?

Dr. Bode:

Right, yes, there's good data showing that it works for viruses as well and preventing some viruses to enter the system. We have some data on protozoan parasites that occur that does not attach to epithelial cells and cannot kill them anymore. There's data from our lab in collaboration with Cheryl Gale in Minnesota showing that they have effect on fungi, so really yeast protective, which is very important for the NICU. So, there is all kinds of organisms, not just bacteria that oligosaccharides might target and prevent their growth or help them develop in the terms of bacteria that we would like to have in the intestine.

Dr. Bode:

So, Terry, how important are human milk oligosaccharides for immune development for the newborn?

Ms. Johnson:

Well, we've talked some about that, but I think one of the most interesting areas is in the development of the microbiome. The microbiome, of course, has been looked at as the largest component of immunity that we develop in postnatal life, and it contributes throughout the lifespan to the health of the individual. What's interesting is that these human oligosaccharides, as we've said, they function as a prebiotic. They are food not for the baby but for the emerging microbiota that is occupying the gut and that will be interactive with foreign bacteria throughout life. The amount and composition differ between term infants and preterm infants as far as the availability in human milk of these human oligosaccharides. We see a higher concentration in preterm women's milk than we do in the term infants, and we also just see a larger component and diversity of these various immune agents in the milk.

The benefits of donor human milk is such that you do get this hyperimmune amount of human oligosaccharides that may, in fact, interact very differently than just the ones that are specific between one mom and one baby. The cow's milk products, the issue is the relative unavailability of human milk oligosaccharides that can be passed on in those feedings at this time. A mother's own milk is preferred because of its specific nature, because of its gestational appropriateness for that particular infant in providing HMOs.

Dr. Bode:

We talked about the microbiome and the different effects of human milk oligosaccharides. Can you put those two things together? How might human milk oligosaccharides determine microbiome composition in the infant, in the newborn?

Ms. Johnson:

What we know about microbiome development in babies, it has much to do with two factors. The first is going to be mode of delivery, how the baby was born. Was he a vaginal delivery or was he born by Cesarean section? The second is going to be diet. In the first we call it almost an inoculum. The baby with a vaginal decent exposure at the time of rupture of membranes in delivery literally gets bathed in his mother's microbiota and in the resident microorganisms that are living in her vaginal and GI tract at the time of delivery. Those move into the baby's mouth, on to the skin. They move throughout the baby's system. And by 24 hours of age, we pretty much think of the gut as being seeded, as it were, with maternal microbiome. The difference happens when there's a Cesarean section delivery. In Cesarean section delivery, especially around the preterm infant population, many things happen that don't contribute to normalization of the microbiome development. First is going to be the fact that there's usually not rupture of membranes. And in preterm deliveries, very, very common for them to both be by Cesarean section, so the infant has no contact whatsoever with the maternal microbiota or GI flora, and then thirdly, that there's going to be a significant amount of antibiotic exposure. Frequently, mothers who are high-risk at the time of delivery may be presenting with an inflammation, may have a chorioamnionitis. Those moms are on broad-spectrum antibiotics, and their infants may be as well. Those very much disrupt the normal process of development of the microbiome. The second factor has to do with diet, and as we've been saying, human milk is unique in that it provides these oligosaccharides that feed the growing microbiota that the infant receive from his mother, and so diet is the second big influence after the establishment of the microbiome at the time of delivery.

Sharon, is there anything else related to infant immunity and digestive function that we should discuss today?

Dr. Groh-Wargo:

Well, Terry, as I said before, I think of human milk as a food, but it is just loaded with not only these human milk oligosaccharides, which function as antiinflammatory and antimicrobials, but there are a host of other antimicrobials and antiinflammatory constituents including nucleotides and cytokines and lysosomes. Really, there are literally hundreds. In addition to those, there are also hormones that are present in the human milk, including insulin and prolactin, and several digestive enzymes, including lipases and amylase. I mean, when you look at the digestibility of the fat in human milk, we know that it has not only to do with the way the triglyceride molecule is formulated but also the fact that these digestive enzymes are present right in the milk, and fat is a hugely important nutrient for babies.

In addition to all of those, there's also transporters for a variety of nutrients and other biologics. There are growth factors, epidermal growth factor, and miscellaneous other sort of nonnutritive components including carotinoids. That's what makes colostrum its beautiful color, but carotinoids are in human milk throughout the stages of lactation. So, really, it is a very complex biological fluid and contains the three macronutrients and all the micronutrients, but this just array of factors that are very bioactive and very protective for newborns.

Dr. Bode:

The list of the bioactive components in human milk is growing and growing. It's really fascinating to see that this is not just a fluid. Like you said, it is there to serve with nutrients, but it's really a tissue. There's immune cells that come with human milk, and we don't really know what they do at this point. There are stem cells in human milk that might be transplanted into the infant, a very hot topic of research at this point.

I'd like to emphasize one point, that it's not just the effect, the immediate short-term effect on the newborn that human milk addresses, but it's really the long-term effect as well, which is this whole concept of DOHAD, the Developmental Origins of Health and Disease, where you do something during pregnancy and lactation that then impacts health and disease risks later on in life for the infant that then is in the second, third or fourth decade of life. So, human milk not only has an impact on the newborn immediately when it's fed, but really, it sets the stage for health and disease later on in life and really has an effect on diseases like diabetes, obesity, asthma, allergies, all those kinds of things that we're dealing with where human milk might already have an impact on.

Ms. Johnson:

I think that was so vividly displayed in the metaanalysis that accompanied the 2012 recommendation from the American Academy of Pediatrics for the use of human milk, was that they were able to show from infancy through adulthood lifelong benefits that come from exposure to this human milk immune product across the lifespan with even sometimes just days of exposure to up to months to a year of exposure, that its ability to continue to protect extends far beyond the first months of life.

On behalf of my colleagues Dr. Lars Bode and Sharon Groh-Wargo, I'm Terry Johnson, neonatal nurse practitioner. Thank you so much for joining us today.

Announcer Close

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