DSM Symposium

Abstract Booklet

Building a foundation for infants' health: The role of LCPUFAs & HMO innovations

THURSDAY, 23 JUNE 2022, FROM 18:15 - 19:15

AUDITORIUM 15

CHAIR AND SPEAKERS:

José Manuel Moreno-Villares
Spain

Berthold Koletzko
Germany

Sharon Donovan
USA

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18:15 Introduction from our Chairman

José Manuel Moreno-Villares MD, PhD

Department Pediatrics. Clínica Universidad de Navarra. Spain

Jose Manuel Moreno-Villares (Madrid, Spain 1961) received his M.D and PhD in Complutense University, Madrid, Spain. He completed his residency in Pediatrics in Hospital 12 de Octubre in Madrid, where he was trained in Pediatric Gastroenterology and Nutrition (1987-1991). He completed a postdoctoral fellowship at the University of California Los Angeles of Medicine (10992-1993) before joining the faculty in the Department Pediatrics of hospital 12 de Octubre where he remained as Associate Professor till November 2017. He is currently Chief of the Pediatric Department in Clínica Universidad de Navarra (Spain) and Associate Professor of Medicine in Universidad de Navarra.

His main interests are Home artificial Nutrition, nutrition support in the pediatric critical care, eating disorders as well as Education in Pediatric Nutrition. He is also devoted to Bioethics, especially in the pediatric setting. http://orcid.org/0000-0003-1513-6579; ID Researcher AAD-8112-2020.

Dr. Moreno has over 300 peer-reviewed publications and more than 80 book chapters. He was the former President of the Committee on Nutrition of the Spanish Pediatric Society. Since 2006 is the Chief Editor of Nutricion Hospitalaria. He has been recipient of numerous awards throughout his career.

Abstract

The first 1,000 days of life - the time spanning between conception and one's second birthday - is a unique period of opportunity when the foundations of optimum health, growth, and neurodevelopment across the lifespan are established. Early life experience influences health determinants through adulthood, and exerts permanent programmed effects on long-term physiology and function. Potential mechanisms of early life programming have been identified involving genetic and environmental factors, with nutrition being a predominant influencer.

Exclusive breastfeeding is strongly associated to decreased prevalence on some childhood infections and diseases, improved immune status as well as cognitive development and decreased risk of Non-Communicable Diseases (NCD) later in life. Knowledge of the complex composition of human milk is increasing, with new components identified.

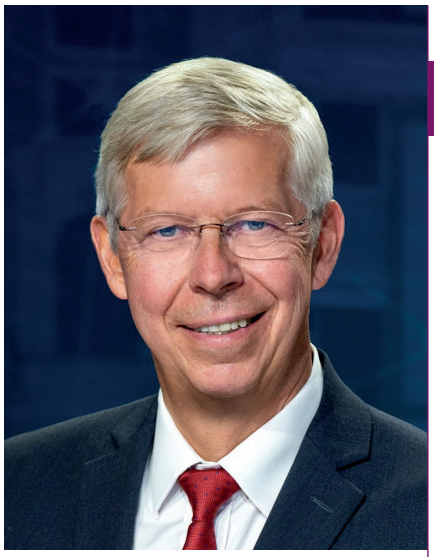
Intestinal microbiota enhances maturation and functioning of the immune system. The interactions between host and intestinal microbiota are potential factors influencing early programming of the intestinal function. The gut microbiota directly influences host metabolism and homeostasis. The establishment of the signature core microbiome begins in early life and is associated with both maternal pregnancy-related factors and early life events, such as type of delivery, type of feeding, gestational age antibiotic exposure, and ecological factors.

While the human brain continues to develop and change throughout life, the most rapid period of brain growth and its period of highest plasticity is in the last trimester of pregnancy and the first two years of life. At birth, rapidly developing brain areas include the hippocampus and the visual and auditory cortices. In the first postnatal year, there is rapid growth of the language processing areas as well as early development of the prefrontal cortex that will control "higher processing" such as attention, inhibition, and flexibility. The first 1,000 days are characterized by rapid rates of neuronal proliferation (cell numbers), growth and differentiation (complexity), myelination, and synaptogenesis (connectivity).

While all nutrients are important for human development and function, optimal overall development depends on providing sufficient quantities of key nutrients during specific sensitive time periods in these first 1,000 days. Thus, this time period harbors the greatest opportunity to provide optimal nutrition to ensure normal development and also the time of greatest vulnerability to any nutrient deficit. Early life, characterized by plasticity, is the ideal time to intervene and to prevent the risk of suffering a NCD ("window of opportunity").

18:25

Should infants be supplied with both omega-3 DHA and omega-6 arachidonic acid?



Prof. Berthold V. Koletzko

LMU - Ludwig Maximilians Universität München, Dept. Paediatrics, Dr. von Hauner Children's Hospital, LMU University Hospitals, Munich, Germany

Bert is Else Kröner-Seniorprofessor of Paediatrics at LMU - Ludwig-Maximilians-University Munich, Dept. Paediatrics, Dr. von Hauner Children's Hospital, LMU University Hospitals, Munich, Germany. He was trained in paediatrics at Baragwanath Hospital, Johannesburg-Soweto, South Africa; Kilimanjaro Christian Medical Center, Moshi, Tanzania; and the Children's Hospitals of the Universities of Düsseldorf, Germany and Toronto, Canada. A focus of his work is on metabolic and nutritional modulators of child health and disease prevention. Bert is author of 1122 scientific journal articles (Web of Science H-index 91, 32,096 citations), 246 book chapters, and 45 books/monographies. His research funding exceeded 20 Mio.€ during the last decade and was provided by the European Union (EU) Framework Research Programmes, EU Research Council, EU Erasmus+ Programmes, EU Joint Programming Initiative, German Research Council, German Federal Ministry Education & Research, German Ministry of Health, Alexander von Humboldt Foundation, US National Institutes of Health, German Academic Exchange Service, Else Kröner Fresenius Foundation, Family Larsson Rosenquist Foundation, and other funding bodies. Bert was rated "World Expert" in research on Breast Milk and Milk (higher than top 0.01 % researchers worldwide based on publications in the last decade, Expertscape 2021) and the world's top rated in the areas "infant nutritional physiological phenomena", "child nutritional physiological phenomena" and "child nutrition science".

Bert is President, Int Soc Res Human Milk & Lactation; Strategic Advisor on Nutrition and Standing Committee Member, Int Pediatric Association; Chair, Secondary-Tertiary Care Council and Executive Committee Member, European Academy of Paediatrics; Treasurer, United European Gastroenterology; Chair, Committee Nutrition, German Society Pediatrics; and Board of Directors Member, Biomedical Alliance in Europe. He served as member of the grant review board medicine, German Research Council (Deutsche Forschungsgemeinschaft), and as chair and deputy chair of their Clinical Trial grant review board. He is Past President of Federation Int Soc of Paediatr Gastroenterol, Hepatol & Nutrition (FISPGHAN) and of European Soc of Paediatr Gastroenterol, Hepatol & Nutrition (ESPGHAN). Bert is Editor in Chief of Ann Nutrition & Metabolism and of World Rev Nutrition & Dietetics, and Associate Editor of Curr Opin Clin Nutr Metabol Care and Monatsschrift Kinderheilkunde. He has been acting as Scientific Advisor to the German Federal Government, the Innovation Initiative of the Chancellor of the Federal Republic of Germany, the European Commission, the European Parliament, the World Health Organisation, the Food and Agriculture Organisation of the United Nations, and other national and international governmental bodies and organisations.

Abstract

Humans need a regular supply of essential omega-3 (n-3) and n-6 polyunsaturated fatty acids (PUFA) to support health. Infants have high PUFA requirements due to added needs for growth. They also deposit relatively large amounts of long-chain PUFA (LC-PUFA), predominantly n-3 docosahexaenoic acid (DHA) and n-6 arachidonic acid (ARA), in membrane rich tissues e.g. brain and immune cells. Infants have a limited capacity for PUFA conversion to n-3 DHA and n-6 ARA not matching utilization, hence infants fed formula without LC-PUFA develop postnatal LC-PUFA depletion associated with adverse functional consequences (1). Common polymorphisms in the fatty acid desaturase (FADS) gene cluster predict PUFA conversion activity. About 30 % of European and about 70 % of Asian and Latin American populations carry the FADS haplotype A resulting in inactive PUFA conversion[2]. Human milk always provides preformed DHA (mean ≈0.3 % of fatty acids) and ARA (≈0.5 %) considered to cover the LC-PUFA needs of term infants. ARA and DHA contents were found correlated in human milk of mothers of term[3] and preterm infants[4], with mean ARA:DHA-ratios of 1.8 in both Europe and North America[3, 4]. Breastfeeding providing LC-PUFA, vs. formula that does not, induces higher LC-PUFA contents in blood and tissue lipids, higher intelligence test scores at the age of 8 years, and less doctor diagnosed asthma up to the age of 10 years, with amplified effects in infants carrying the FADS haplotype A compared to haplotype D[5, 6]. The interaction of LC-PUFA supply with genotype in predicting clinical outcomes supports a causal role of early life LC-PUFA availability for later intelligence and asthma risk (Mendelian randomization). FADS haplotype variation markedly affects ARA status but has little impact on n-3 LC-PUFA status[2, 7], thus n-6 LC-PUFA status seems relevant for clinical outcomes. Randomized clinical trials documented the safety of adding DHA and ARA to infant formula, and several but not all reported functional benefits. The European Food Safety Authority concluded that a cause-effect relationship was established between breastfeeding or feeding a formula containing at least 0.3% of fatty acids as DHA in infancy, and visual development[8]. Regulatory standards in the European Union now require infant and follow-on formula to contain 20–50 mg DHA/100 kcal[9], with DHA between 0.33 and 1.14 % of fat at the permitted fat content of 4.4-6 g/100 kcal, or 0.38-0.94 % at a mean fat content of 5.2 g/100 kcal. This leads to generally higher DHA contents in formula than typically found in human milk, and in infant formula products evaluated and used so far, however without the need to also include ARA. This novel concept of infant formula composition raised concerns and controversy. International experts in the field of infant reviewed current evidence and provided recommendations[10]. Most clinical trials exploring safety and benefits of LC-PUFA enriched formulas evaluated DHA levels near 0.3% along with higher or similar ARA contents. Formula feeding with decreasing ARA:DHA-ratios led reduced ARA contents in some brain areas in non-human primates[11], and after infant feeding attenuated neurodevelopmental outcomes in later childhood[12]. Blood analysis showed increased DHA with higher DHA intakes, whereas ARA levels showed a strong inverted-U function in response to decreasing ARA:DHA-ratios. Reduced ARA may be responsible for the reduction in benefit on cognitive outcomes[13]. Therefore, the panel concluded:

- Infant and follow-on formula with high DHA contents but no ARA deviate markedly from human milk composition, and their safety and suitability has not been established.
- Based on current evidence, infant and follow-on formula should provide both DHA and ARA.
- Formula DHA should reach at least mean contents in human milk (0.3% of fatty acids) and preferably 0.5%.
- Based on current knowledge ARA provision along with DHA is strongly recommend. At DHA levels in infant formula up to ≈0.64%, ARA contents should at least equal DHA contents.
- Further well-designed clinical studies should evaluate the optimal intakes of DHA and AA in infants at different ages based on relevant outcomes.

18:45 Human Milk Oligosaccharides in Early Life as Modulators of Infant Development

Prof. Sharon Donovan

Department of Food Science and Human Nutrition, University of Illinois, Urbana, IL USA

Dr. Donovan received her Ph.D. in Nutrition in the laboratory of Bo Lönnerdal at the University of California at Davis. She completed a postdoctoral fellowship at the Stanford University School of Medicine before joining the faculty in the Department of Food Science and Human Nutrition at the University of Illinois, where she is currently Professor and Melissa M. Noel Endowed Chair in Nutrition and Health. In 2020, she was named the inaugural Director of the Personalized Nutrition Initiative at the University of Illinois.

Her laboratory conducts basic and translational research in the area of pediatric nutrition. On-going work is focusing on nutritional approaches to optimize the development of the gut microbiome and gut, immune, cognitive development in infants.

Dr. Donovan has over 250 peer-reviewed publications and has garnered over $35M in grant support from the NIH, USDA, foundations, and the food and pharmaceutical industry. Dr. Donovan was a member of the 2020-2025 Dietary Guidelines for Americans Scientific Advisory Committee. Dr. Donovan served as President of the American Society for Nutrition (2011-2012) and the International Society for Research in Human Milk and Lactation (2018-2020). She has been recipient of numerous awards throughout her career and was elected to the U.S. National Academy of Medicine in 2017.

Abstract

Human milk is a complex biological fluid that contains nutrients and non-nutritive bioactive components that nurture the immune, microbiome and neurocognitive development of the infant. Among the bioactive components are the human milk oligosaccharides (HMOs), which constitute the 3rd most predominant solid component of human milk. HMO are synthesized in the mammary gland via elongations of lactose with one or more of the following monosaccharides: galactose, N-acetyl-glucosamine, fucose, and sialic acid. HMOs vary widely between individuals and across global populations, due largely to differences in maternal genetic factors influencing glycosylation patterns (FUT2 – Secretor gene and FUT-3 –Lewis gene). Preclinical and clinical evidence support diverse actions of HMOs in supporting infant health and systems development. HMOs are resistant to digestive enzymes and maintain intact structures within intestine, where they serve as prebiotics for specific strains of bifidobacteria and bacteroides, improve gut barrier function, inhibit binding of pathogens, and reduce the risk of necrotizing enterocolitis. Additionally, systemic effects of HMO on immune and neurocognitive development have been reported. To date, seven synthetic HMO (2'-FL, 3-FL, DFL, LNnT, LNT, 3'-SL, 6'-SL) have received Generally Recognized As Safe (GRAS) status in the U.S. and also have positive opinions from EFSA regarding their safety. Term infant formulae were initially supplemented with one (2'-FL) or two (2'-FL + LNnT) HMO, but newer formulas contain 5 to 6 HMO. This presentation will review the levels and variation of HMO in human milk and will provide a critical assessment of the existing observational evidence for HMO activities within the context of human milk on infant outcomes on weight gain and neurocognitive outcomes. In addition, the findings of randomized, placebo-controlled clinical intervention trials of HMO supplementation to infant formula on tolerance, growth, immune, and microbiome outcomes will be summarized. Overall, these studies have demonstrated safety of HMO and the potential for modulation of plasma cytokines outcomes, antibiotic and antipyretic use, and parent-reported morbidities. Potential mechanisms of action of HMO, including findings from recent applications of systems biology and machine learning approaches, will be presented. Lastly, potential future opportunities for HMO clinical for preterm infants and as well as for atopic disease prevention will be proposed.

19:05 Questions & Answers session

José Manuel Moreno-Villares

Prof. Berthold V. Koletzko

Prof. Sharon Donovan

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