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SATELLITE SYMPOSIUM

A SPOTLIGHT ON THE ROLE OF LIPIDS IN EARLY LIFE NUTRITION; PAST, PRESENT AND FUTURE

18 May 2023, 14:00-15:00
Parallel D, Level -2



CONTENT OVERVIEW

SPEAKERS

Prof. Susan Carlson
US

Prof. Cristina Campoy
Spain

Assoc. Prof. Ardy van Helvoort
The Netherlands

SYMPOSIUM AGENDA

TIME	TOPIC	SPEAKER
14:00	**Welcome and introduction**	*Prof. Susan Carlson (US)*
14:05	**History of lipids in early life: Looking back into the PAST**	*Prof. Susan Carlson (US)*
14:20	**The importance of Lipids: Eyes on the PRESENT**	*Prof. Cristina Campoy (Spain)*
14:40	**Next generation Lipids to support healthy growth and development in early life**	*Assoc. Prof. Ardy van Helvoort (The Netherlands)*
15:00	**Close**	

This symposium is not included in the main event CME/CPD credit.

For Healthcare Professionals only.

PROF. SUSAN CARLSON

AJ Rice Professor of Nutrition, Department of Dietetics and Nutrition

University Distinguished Professor

University of Kansas Medical Center

Carlson received her bachelor's degree in home economics at Washington State University in 1969 and her doctorate in nutrition with minors in biochemistry and physiology from Iowa State University in 1975. She had NIHLB postdoctoral fellowships at the University of Wisconsin in the Department of Pathology (1975-1977) and at the University of South Florida in the Department of Pediatrics (1978-1979).

As a faculty member in several medical school departments of pediatrics, mainly in divisions of newborn medicine from 1979-1997, Carlson rose through the ranks to professor in the Departments of Pediatrics, Obstetrics and Gynecology and Biochemistry at the University of Tennessee, Memphis, Tenn. Her major research interest during those years was on the effects of fatty acids that compose a large percent of brain membranes and are found in human milk but not in vegetable oils typically used in the production of U.S. infant formulas.

After moving to Kansas City in 1997, she continued her research on the effects of docosahexaenoic acid (DHA) and arachidonic acid (ARA) on brain development in term infants in collaboration with a team of cognitive and neuroscientists. She also conducted studies of DHA supplementation during pregnancy and infant/child development. Most recently, her group showed that DHA dramatically reduced the risk of early preterm delivery (<34 weeks gestation) and preterm delivery (<37 weeks gestation).

Professional Affiliations and Major Awards

- International Society for the Study of Fatty Acids and Lipids, served on the Executive Committee from 2005-2015. Past President, 2015 - 2018
- American Society for Nutrition, 1984 to Present, Consulting Editor, 2005 – 2010. ASN Fellow 2021
- American Pediatric Society, Member, 1996 – Present. Currently Emerita
- American Oil Chemists Society, Member, 1991 – 2006
- Honorary member of the Academy of Nutrition and Dietetics for pioneering work in the role of DHA in infant development 2002
- March of Dimes Agnes Higgins Award for pioneering research benefiting women and children 2008
- Who's Who Albert Nelson Marquis Lifetime Achievement Award 2019
- International Society for the Study of Fatty Acids and Lipids (ISSFAL) Alexander Leaf Award 2021
- Global Organization for EPA and DHA Omega-3s (GOED) Lifetime Achievement Award 2022

Publications

- More than 200 peer-reviewed publication and chapters and over 200 national and international invited lectures for industry, government, scientific organizations and university/government/ foundations and institutes

ABSTRACT

History of lipids in early life: Looking back into the PAST

Human milk from a well-nourished mother is the recommended sole source of nutrition for infants up to 6 months of age, with continued breastfeeding thereafter in conjunction with appropriate complementary feeding until 2 years of age or beyond. While the macronutrient quality and quantity of human milk changes over time, approximately 50% of the energy from all mature human milk comes from lipids.

Infant formulas were designed to meet the needs of infants who were not breastfed, and formulas throughout the 20th century considered human milk lipid quantity, but not quality, as a model for how much lipids to add to infant formula. In the early 1980s, we began to understand that lipid quality of human milk should be considered.

The story began when we discovered that the vegetable oils used to provide the lipids in infant formula did not provide the long chain omega-3 fatty acid, docosahexaenoic acid (DHA) or the long chain omega-6 fatty acid, arachidonic acid (ARA). There were obvious reductions in red blood cell membrane DHA and ARA in infants fed formula compared to human milk. At the same time, DHA was beginning to be understood as a physiologically important fatty acid. To this day, DHA is the most studied lipid in human milk.

Global and national/regional standards are periodically updated with the intention of improving guidelines. Changes are based on emerging scientific insights on functional and compositional properties of fatty acids in nutrition and/or infant requirements. In 2002, DHA and ARA were added to infant formulas in the United States and nowadays most infant formulas in the US contain both. In Europe however, all formulae must contain DHA in higher amounts than found in human milk without the need to also include ARA. International experts published a position paper and concluded that both quality and quantity of lipids are important and ARA should be mandatory in formula. However this is not the case as of today.

Our understanding of the functional role of some human milk lipids continues to evolve as does the composition and physical properties of infant formulas. This is the topic to be presented by the next two speakers.

PROF. CRISTINA CAMPOY

Head of the Department of Paediatrics. Faculty of Medicine, Avda. de la Investigación, 11 -18016 - Granada

Director of the EURISTIKOS Excellence Centre for Paediatric Research, Health Science Technological Park

Campoy received her bachelor in Medicine and Surgery by the University of Granada (UGR) in 1986 and her doctorate by the UGR in 1989. She became professor of Paediatrics at UGR in 1989. Since 1990, she is the person in charge of the Research Group-PAI -CTS-187 on: "Nutrition and Metabolism in Paediatrics". She specializes in Paediatrics, and is an expert in Neonatology (1997) and Paediatric Endocrinology and Nutrition (1998).

Professional Affiliations

- Member of the ESPGHAN Committee on Nutrition (2011-2017).
- ESPGHAN representative at the EU Platform for Action on Diet, Physical Activity and Health.
- European Commission.
- Member of the Committee on Nutrition of the Spanish Association of Paediatrics (AEP)
- Member of the Nutrition Expert Group of the SEGHNP
- Coordinator of the FP7 NUTRIMENTHE EU Project and the PREOBE Excellence Research Project; UGR principal investigator of the IMPACT DIABETES B2B, PREciSE, DynaHEALTH, EarlyNutrition, MyNewGut, NutriOMICs, EARNEST and NUHEAL EU Projects, PREOBE, GDBrain, EVASYON and member of CIBERESP-ISCIII.
- Coordinator of the Official Interuniversity Master on "Genetic, Nutritional and Environmental factors for Growth and Development" (NUTRENVIGEN-G+D Factors).
- Member of the Royal Academy of Medicine of Granada, Spain
- Member of the Royal Academy of Pharmacy of Catalonia, Spain
- Member of the Spanish Academy of Nutrition and Food Sciences
- Editor of Frontiers in Nutrition, topic Nutrition & Brain; Editor of Nutrients issue: Early Nutrition and reprogramming of health and disease; Editor of Nutrients issue: Nutrition and gut-brain axi
- Referee of numerous journals: Am J Clin Nutr, Metabolism, Frontiers in Nutrition, Frontiers in Pediatrics, Nutrients, JPGN, Br J Nutr, J Pediatr, Pediatr Res,...

Publications

- More than 300 papers & chapters in National-International Journals and books, more than 620 abstracts and numerous Conferences in National and International Meetings

ABSTRACT

The importance of Lipids: Eyes on the PRESENT

Lipids play a critical role in early life, for growth, brain development, cognitive function, gastrointestinal and immune development and function. They are an important source of energy for vital organs, essential for the formation of cell membranes and for the synthesis of hormones and signaling molecules that regulate cellular processes.

Infants who are exclusively breastfed receive a significant amount of lipids in the form of human milk fat, which contains essential fatty acids (EFA) {linoleic acid (LA, omega-6) and -linolenic acid (ALA, omega-3)}, long-chain polyunsaturated fatty acids (LCPUFAs), and lipid soluble vitamins with biological effects in early life. Furthermore, human milk (HM) contains complex lipids and milk fat globules (lipid droplets surrounded by a phospholipid tri-layer referred to as milk fat globule membrane (MFGM)) with important bioactive properties.

EFA and LCPUFAs are provided by HM or supplemented infant formula when breastfeeding is not possible. Moreover, LCPUFAs can also be endogenously synthesized, although this process is very slow during early life. FADS and ELOV gene clusters code for enzymes that catalyze the desaturation and elongation steps, respectively, of which some specific enzymes (D5D, D6D) encoded by specific genes (FADS1, FADS2) are rate-limiting in the conversion and the biosynthesis of LCPUFAs (crucial in early life). As a consequence, infants have important needs of DHA and ARA, and those with specific genotypes may require different amounts of LCPUFAs to maintain an adequate status. The new European regulations would compromise the LCPUFAs status specially in infant populations were the incidence of “non-beneficial” FADS polymorphisms is very high, like in Latin America.

The brain is primarily composed of lipids, and specifically of EFA and LCPUFAs, such as omega-6 arachidonic acid (ARA) and omega-3 docosahexaenoic acid (DHA). These lipids are essential for growth, function of neurons and synapses, and serve as building blocks for myelin. In addition, pre- and post-natal LCPUFAs supply can influence gut microbial composition, visual acuity scores, psychomotor and cognitive outcomes (memory, attention, and language development), brain functioning and reduced risk of developmental delays in the offspring. MFGM in infant formulas may support brain development by promoting the growth of neural cells and changing brain structure and neurocognitive functioning. MFGM supplemented to an infant formula, together with LCPUFAs, and synbiotics can help to mimic the nutritional and functional properties of HM. The provision of MFGM may reduce infections, inflammation and promote a slower maturation of the gut microbiota as seen in breastfed babies.

In the last years, new technologies are expanding the possibilities to add new bioactive compounds like LCPUFAs, MFGM, HMOs, Biotics, nucleotides, osteopontin, lactoferrin, lutein,.. , etc. to infant formulas, bringing structural and functional properties much closer to HM. However, more studies are needed to understand how to further optimize and personalize lipid composition in infant formula.

ASSOC. PROF. ARDY VAN HELVOORT

Senior Director Research & Innovation - Centre of Excellence Nutritional Physiology & Functional Nutrients Danone Nutricia Research, Utrecht, The Netherlands

Associate Professor Medical Nutrition & Metabolism in Disease Management, NUTRIM, School of Nutrition and Translational Research in Metabolism, Faculty of Health, Medicine, and Life Sciences, Maastricht University Medical Center+, Maastricht, The Netherlands

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Van Helvoort received his MSc degree in biology from Wageningen University and obtained his PhD in cell biology from the Faculty of Medicine, Utrecht University, the Netherlands in 1996. He worked as a researcher at the Netherlands Cancer Institute in Amsterdam till 1999, and then joined Numico Research in the Netherlands where he was responsible for various (pre)clinical research projects. In 2008, he became the Research Director Disease Targeted Nutrition for oncology, COPD, HIV, renal failure and diabetes. From 2011 to 2014 he was responsible for the Asian R&D activities for Medical Nutrition. Since then he has been leading the life science platforms on Nutrition, Muscle and Neuroscience for Danone Nutricia Research and as of 2019 the Growth and Metabolism team. Next to that Van Helvoort holds a position at Maastricht University in the field of nutrition and integrated care since 2015.

Publications

- More than 75 full peer reviewed papers.

ABSTRACT

Next generation Lipids to support healthy growth and development in early life

Exclusively breastfed infants have the best start in life in terms of growth quality & metabolic development. As such breastfeeding may protect against later life obesity and Non-Communicable Diseases.

Human milk (HM) is rich in lipids which are, amongst others, important for growth, brain- and cognitive development. In HM, these lipids appear as large lipid droplets with a mode diameter of ~4 µm, enveloped by a complex triple-layered membrane mainly consisting of glycerophospholipids, sphingomyelin, glycosphingolipids, cholesterol, and specific membrane proteins.

These highly complex and unique lipid structures define the specific digestion and absorption kinetics of HM lipids. The lipid droplets present in standard infant formulas are generated through traditional processing and are different in the overall lipid composition, the structure of triglycerides, the lipid membrane coating, as well as the droplet size (mode diameter <0.5 µm). It is hypothesized that these structural differences may affect lipid digestion and absorption in infants and consequently affect metabolic response and brain development. This may partially explain the difference in growth and body composition and cognitive development between human- and formula fed infants and the subsequent longer-term differences in risk for metabolic health complications or disorders in later life.

Danone Nutricia Research has developed a unique process to produce a concept infant formula with large, milk phospholipid coated lipid droplets (mode diameter 3-5 µm; NUTURIS) (Gallier et al., 2015) that mimic the physical properties of lipid droplets present in HM. NUTURIS brings the compositional, structural and functional properties of infant formula closer to those of HM. In European and Asian infants, NUTURIS has been shown to be safe and well-tolerated, and ensures growth according to WHO standards. During this ESPGHAN congress we present different outcomes from the NUTURIS experimental research and clinical study program on long-term growth, metabolism and brain development.

ABSTRACTS ESPGHAN 2023

Abstract oral presentation **Date:** 18/05/2023 **Time:** 18:15-19:15		
Infant milk formula with postbiotics reduces visceral hypersensitivity, potentially by affecting the serotonin and ahr signaling pathways	**N. IJssennagger**, Fernanda Olguin-Diaz, Mona Mischke, Valerie Tondereau, Vassilia Theodorou, Jan Knol, Ingrid B. Renes, Helene Eutamene	We previously reported that partly fermented infant milk formula (IMF) lowers the incidence of infantile colic in healthy term-born infants. However, mechanistic insight in how this IMF with postbiotics impacts gut homeostasis is limited. Our data suggests that certain metabolites that are higher in IMF with postbiotics, such as IML and ILA, influence AhR and serotonin signaling pathways and might thereby influence visceral sensitivity.
Abstract oral presentation **Date:** 19/05/2023 **Time:** 08:30-10:00		
Tolerance development in cow's milk-allergic children receiving amino acid–based formula with synbiotics: 36 months data of a randomized controlled trial (presto study)	P. Chatchatee, A. Nowak-Wegrzyn, L. Lange, S. Benjaponpitak, K. Wee Chong, P. Sangsupawanich, M. van Ampting, M. Oude Nijhuis, J. Langford, S. Eussen, V.Trendelenburg, R. Pesek, C. Davis, A. Muraro, M. Erlewyn-Lajeunesse, A. Fox, L. Michaelis and K. Beyer on behalf of the PRESTO study team	The proportion of children who developed tolerance to cow's milk (CM) 36 months after the start of a 1-year intervention period with amino acid-based formula (AAF) was high (about 75%) and similar for children receiving AAF with or without synbiotics. This proportion is comparable to natural outgrowth of CM allergy. Our data suggest that the consumption of AAF and absence of exposure to CM peptides do not slow down CM tolerance acquisition.

ABSTRACTS ESPGHAN 2023

Abstract e-poster presentation		
The physical properties of lipid droplets in infant formula affect metabolic and brain function in mouse models	A.Oosting, L. Harvey, S. Ringler, G. van Dijk, L. Schipper	We demonstrated that early life exposure to Infant formula (IF) with lipid droplets that closely mimic the physical structure of lipids in Human milk (HM) promote organ omega-3 LCPUFA status during development and improved metabolic health and cognitive function later in life. These data suggest that the physical properties of dietary lipids in IF can further improve growth, metabolic health and neurocognitive development of formula fed infants.
Infant formula with large, milk phospholipid coated lipid droplets modulates gut epithelial lipid profiles differently from standard infant formula and closer to human milk	M. Mischke, F. Daouad, G. Thomassen, J. Knol, I. Renes	Exposure to Human Milk or Nuturis lead to similar lipid profiles in gut epithelial cells in an in vitro gut model. Standard infant formulas with small, protein-coated lipid droplets, even with added MFGM phospholipids, show different effects on lipid profiles, underlining the relevance of lipid globule size and coating as opposed to sole lipid composition. Distinct lipid profiles likely link to lipid functionality in the gut, and in turn to lipid partitioning throughout the body, possibly affecting growth, metabolism and brain development.
In vitro lipid bio accessibility rate of infant formula with large phospholipid coated lipid droplets is slower than standard infant formula and closer to human milk	G. Thomassen, E. Abrahamse, M. Mischke, M. Becker, J. Knol, I. Renes	Nuturis infant formula (IF) lipid handling during gastrointestinal transit is different from standard IF, resulting in a slower lipid bio accessibility rate, which is closer to that of human milk (HM). A slower lipid bio accessibility rate is hypothesized to lead to lower postprandial plasma lipid levels, which can impact lipid partitioning, metabolism and growth.
Structural changes of infant formula with large phospholipid-coated lipid droplets during invitro digestion are closer to human milk than standard infant formula	Wei Wei, J. Gan, E. Abrahamse, I. Renes, N. Bartke X. Zhao, X.Wang	Milks with different fat droplet size and structure modulate lipid digestion. The characteristics of lipid digestion of Nuturis and human milk (HM) are alike, showing similar structural changes during gastric phase and comparable shifts of lipolysis degree in the gastric/intestinal phase.
The use of growth artificial intelligence algorithm for length estimation (GAIN) of children in real-world settings	M.C. Chua, M. Hadimaja, S.Mukherjee, J. Wong, A.Foussat, F.Yap	An artificial intelligence algorithm was built using image recognition technology to estimate the length of children lying on supine positions using data collected in GAIN Study.

ABSTRACTS ESPGHAN 2023

Abstract poster presentation		
Tolerance and safety of an anti-regurgitation formula containing locust bean gum, pre- and postbiotics: an international multicenter prospective randomized controlled trial in infants with regurgitation.	**S. Salvatore**, V. Klymenko, Y. Karpushenko, M. Durczak-Hilleman, A. Loboda, V. Petrashenko, W.Olechowski, G. Lista, F. Meneghin, S. Amodio, A. Bongers, T. Ludwig, Y. Vandenplas	The Anti Regurgitation (AR) formula containing Locus Bean Gum did not lead to more loose or watery stools than the control formula. Both products were well-tolerated and safe. The AR formula showed a significantly lower regurgitation frequency as compared to the control formula.
Digestive tolerance and safety of an anti-regurgitation formula containing locust bean gum, prebiotics and postbiotics : a real-world study	M. Bellaiche, P. Tounian, R. Oozeer, E. Rocher, Y. Vandenplas	The Anti Regurgitation (AR) formula was well tolerated and appeared to provide an effective strategy for managing the complete range of issues associated with infant regurgitation and gastrointestinal discomfort in a real-world clinical study setting.
The infant milk formula ingredients milk fat, A2 beta-casein, lactoferrin, and specific prebiotics impact the relative abundance of Proteobacteria in vitro	S. Tims, H. de Weerd, T. Ludwig, X. Zhao, J. Knol, G. Roeselers	Bifidobacterium to Proteobacteria ratios after 24 hour in an in vitro fecal fermentation system, indicate that infant formula with combinations of scGOS/lcFOS, milk fat, A2 beta-casein and/or lactoferrin are likely to beneficially modulate the infant gut microbiota.

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Abstract poster and e-poster presentation		
Infant formula ingredients lutein, beta-palmitate and casein phosphopeptide in combination with scGOS/lcFOS limit intestinal oxidative stress	F. Daouad, N. IJssennagger, L. Schwebel, X. Zhao, J. Knol, I. Renes	The immature intestines of infants are susceptible to oxidative stress, which can lead to gut barrier dysfunction, reduced nutrient absorption and gut inflammation. Our data show that SCFA, derived from scGOS/lcFOS (9:1) fermentation, in combination with either lutein/MAG (derived from beta-palmitate digestion) or lutein/CPP significantly reduce oxidative stress, thereby supporting a well-functioning gut and thus gut health.
Lutein suppresses in vitro ige- and non-ige-induced mediator release by rat basophil-like leukemia (RBL-2H3) cells	A. I. Kostadinova, K. Knipping, N. Buurman, C. Arknaar, I. Dullemond, T. Ludwig, R. Bourdet-Sicard, X. Zhao	Lutein is a dietary carotenoid that can also be found in human milk. Currently, the main known benefits of early life lutein consumption relate to neuro-development. In this study, we found that lutein showed anti-allergic potential in rat basophil-like leukemia (RBL-2H3) cells, a model for mast cell degranulation. Lutein was inhibiting mast cell degranulation in an IgE-dependent and IgE-independent manner. In addition, SCFA improved synergistically the suppressive capacity of lutein. Those results provide a rationale to further investigate dietary interventions with lutein alone or in combination with non-digestible oligosaccharides as a potential strategy to prevent symptoms in (food) allergies or in allergy/inflammatory diseases with mast cell involvement.
Effects of prebiotic-supplemented formula on gut microbiome development in chinese children from 0-24 months: a multicenter decentralized clinical trial during the Covid-19 pandemic	Z. Zeng, M. Liu, G. Roeselers, S. Gong	This study shows that in healthy Chinese infants, an infant and young child formula supplemented with scGOS/lcFOS is correlated with increased relative abundance of Bifidobacterium and Shannon diversity in the age of 0-6 months. In the FF and BF groups (0-6 months, 6-12 months and 12-24 months) we observed a succession in microbiome composition in line with studies conducted in healthy infants in other geographical regions. The decentralized digital platform allowed the study to be carried out remotely during the COVID-19 pandemic.

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