



## **Symposium**

Sunday, 4 August 2019

08:00 – 12:00

# **Micronutrient Composition of Human Milk: New Understanding and Research Options that Advancing Technology is placing at our Fingertips**

**Peter van-Dael, PhD**

DSM Nutritional Products, Kaiseraugst, Switzerland

### **Introduction**

**Noel W. Solomons, MD**

Center for Sensory Impairment Aging and Metabolism, Guatemala

### **Breast Milk Nutrient Analysis – A Two-Way Mirror: Reflections on Infant intake and maternal status**

**Lindsay H Allen, PhD, RD**

USDA, ARS Western Human Nutrition Research Center, Davis, California

### **Revisiting the Adequacy of Micronutrient Intakes in Breast-Fed Infants: Conceptual and Practical Advances toward Universal Standards**

**Maria Makrides and Robert Gibson**

South Australian Health and Medical Research Institute, Adelaide, SA 5000, Australia.

### **How much omega-3 long chain polyunsaturated fatty acids (LCPUFA) do human infant require? What action can be taken to satisfy the need?**

**Robert A. Gibson, PhD**

South Australian Health and Medical Research Institute, Adelaide, SA 5000, Australia.

### **The Basic Human Biology and Epidemiology of Long-Chain Polyunsaturated Fatty Acids (LC-PUFA), with notes on diagnostic analysis**

**Douglas Bibus, MSc, PhD**

University of Minnesota, Minneapolis, MN, USA and Lipid Technologies LLC, Austin, MN, USA

**Beyond the Usual Subjects: The health and developmental implications of the “other” fatty acids in infant nutrition, including arachidonic (ARA) and docosopentaenoic (DPA) acids**

## Breast Milk Nutrient Analysis – A Two-Way Mirror: Reflections on Infant intake and maternal status

Noel W. Solomons, MD

Center for Sensory Impairment Aging and Metabolism, Guatemala

The WHO recommends exclusive breast-feeding for the first semester of infant life. This would only be a safe and reliable recommendation, however, if the composition of human milk were universally adequate in all of the liquid, macro- and micronutrients required for growth and development from 0-6 months. Rather than a question, this has been an assumption. So, by reflex logic, the recommended nutrient intakes have been established based on what is obtained in the consumption 780 mL of milk, with an assigned composition from reference analyses. Interest in milk composition has recrudesced, aided by emergent analytical technology for more precise and accurate quantification, e.g. spectroscopy and isotope-labelling, and by the user-friendly and field-accessible nature of tools such as portable fluorometers or dried breast-milk spotting. When reliably assayed, breast milk micronutrients have the potential to yield information for both infants and mothers: the dietary intake of nutrients, both macro- and micronutrients, can be estimated for the infant making assumptions about milk volume, that is, it becomes about the baby - not the milk - when viewed in this light. The potential for assessment of maternal nutrient environment, either recent diet or nutrient stores, is possible with milk nutrient quantification. This is not a possibility for those nutrient known not to respond to maternal intake and status, but is promising for a set of responsive nutrients such as vitamin A, carotenoids, alpha-tocopherol, selenium, sodium and fatty acids, to name a few. Milk retinol has been used epidemiologically to gauge population hypovitaminosis A.

*Noel W. Solomons MD is a physician and gastroenterologist with 43 years of residence in Guatemala, 34 of those years spent as the Scientific Director of the Center for Studies of Sensory Impairment Aging and Metabolism (CeSSIAM). Recent interests in lactation biology include maternal and milk hydration, milk-microbiome, composition of B-vitamins, minerals, trace element and fatty acids, and nutrition support of human milk by maternal oral supplementation. From 1991-1998, he was visiting instructor at the University of Jakarta. He is the 2002 winner of the Asia Pacific Clinical Nutrition Society. He is Editor-in-Chief of the Food and Nutrition Bulletin.*

## Revisiting the Adequacy of Micronutrient Intakes in Breast-Fed Infants: Conceptual and Practical Advances toward Universal Standards

Lindsay H Allen, PhD, RD

USDA, ARS Western Human Nutrition Research Center, Davis, California

In lactation, micronutrients can be classified into two types. The concentrations of Group I micronutrients (all the B vitamins except folate, all the fat soluble vitamins, choline, and selenium and iodine) in human milk are affected by maternal status and/or intake of the nutrients, and are therefore reduced where mothers consume poor quality diets. Conversely the concentrations of these nutrients may be increased by maternal supplementation. Milk concentrations of Group II micronutrients (folate, iron, copper and zinc) are not affected by maternal nutrition or supplementation. We have developed valid, sensitive and efficient methods for measuring multiple micronutrients simultaneously in human milk and serum. The analytical platforms include UPLC-MS/MS, HPLC, and ICP-MS/MS. We have analyzed milk samples from around the world and revealed great variability in micronutrient concentrations and in responses to maternal supplementation during pregnancy and/or lactation. While concentrations appear to track with the quality of maternal diets i.e. micronutrient density, it has not been possible to define what normal (adequate) micronutrient levels should be. We are therefore leading the Mothers, Infants and Lactation Quality (MILQ) study in well-nourished but unsupplemented mothers in Bangladesh, Brazil, Denmark and The Gambia to develop Reference Values for nutrients in human milk. The output will be percentiles for each nutrient across the first nine months of lactation which, based on the same concept as the WHO reference values for growth, will be useful for interpreting values within and across populations, and the effectiveness of intervention strategies.

*Lindsay H. Allen, PhD, is Center Director, USDA, ARS Western Human Nutrition Research Center in Davis, California. Her research assesses the prevalence, causes and consequences of micronutrient deficiencies, especially vitamin B12 deficiency. She has conducted many studies of the efficacy and effectiveness of micronutrient intervention strategies; food-based, lipid-based nutrient supplements, and fortification. She is currently investigating the quality of human milk - micronutrient adequacy and associations between maternal status, milk and infant status and other outcomes, supported by the Bill & Melinda Gates Foundation. She is Vice-President of the American Society for Nutrition and has many national and international awards.*

## **The Basic Human Biology and Epidemiology of Long-Chain Polyunsaturated Fatty Acids (LC-PUFA), with notes on diagnostic analysis**

**Robert Gibson and Maria Makrides**

South Australian Health and Medical Research Institute, Adelaide, SA 5000, Australia.

The clinical roles omega 3 long chain polyunsaturated fatty acids (LCPUFA) have been the subject of intense research for the last 40 years. Interest arises from the fact that omega 3 LCPUFA, particularly EPA and DHA appear to have actions that oppose those of omega 6 arachidonic acid which are pro-inflammatory. It is now thought that the LCPUFA themselves must be oxidized enzymatically to a range of compounds collectively known as oxilipins (prostaglandins, leukotrienes, resolvins, protectins, maresins) to have biological activity. Despite knowledge of their biochemistry and encouraging data from cellular and animal studies establishing clear clinical benefit in humans has been very difficult. There has been some evidence in support of the anti-inflammatory effects of omega 3 fats in rheumatoid arthritis and the potential protective effects in the prevention of coronary vascular disease has been limited. There is now strong epidemiological support for a role for omega 3 fats in extending gestation and the prevention of preterm birth and several large clinical trials are currently testing this hypothesis. The relationship between clinical outcome and apparent omega 3 status in population studies and clinical trials has been confounded by the high cost of venepuncture, blood processing and the need for cold-chain storage and transport. We have developed a range of systems including dried fluid spot technology that has proven to be ideally suited to the measurement of nutrient status in all biological tissues including blood, plasma, synovial fluid and breast milk. This technology is capable of transforming nutrition studies.

*Robert A. Gibson, PhD is a nutritional biochemist, a Senior National Health and Medical Research Council Research Fellow and Fellow of both the Nutrition Society of Australia and the International Society for the Study of Fatty Acids and Lipids. He has been actively involved in nutrition research in cells, animals and humans for over 30 years, publishing over 300 papers. With a particular interest in human breast milk and has conducted several randomized trials with breast and formula fed infants. He is currently developing a range of dried milk spot tests for the accurate measurement of fat and water soluble vitamins as well as fatty acids and lipids to evaluate the effect of storage of human milk to relate this to clinical outcomes. is Center Director, USDA, ARS Western Human Nutrition.*

## **How much omega-3 long chain polyunsaturated fatty acids (LCPUFA) do human infant require? What action can be taken to satisfy the need?**

**Maria Makrides and Robert Gibson**

South Australian Health and Medical Research Institute, Adelaide, SA 5000, Australia.

The main omega-3 long chain polyunsaturated fatty acid (LCPUFA) in human milk is docosahexaenoic acid (DHA). However, DHA makes up a small proportion of the total fats in human milk with concentrations that are reported to vary from about 0.1% to 1% of total fatty acids. DHA is never absent from human milk, although it varies according to the concentration of DHA in the maternal diet. Maternal DHA dose response studies have demonstrated a linear response to DHA concentration in human milk, without affecting the concentration of other LCPUFA. Assessing DHA in plasma and red cell phospholipids of breastfed babies from these studies indicates that there is a saturation plateau when human milk DHA is at or about 0.8% of total fatty acids. There has been strong interest in understanding how omega-3 LCPUFA, such as DHA, in human milk influence the nutrition and health of infants. DHA is known to have important biological activity that can affect neurological development and the development of allergic disease but determining the optimal DHA in human milk for optimal outcomes has been difficult. It is likely that prenatal supply and the gestational age of the baby at birth affect fatty acid status and outcomes. Relevant studies will be discussed showing that increasing the DHA content of human milk fed to preterm babies better supports short term developmental outcomes, while the developmental outcomes of term born infants may not benefit from extra supplementation.

*Maria Makrides, PhD is Deputy Director at the South Australian Health and Medical Research Institute (SAHMRI) and the Theme Leader for SAHMRI Women and Kids, which is based at the Women's and Children's Hospital and, Adelaide, Australia. As a research dietitian, Maria is committed to improving the nutrition and health of mothers and their babies through the conduct and translation of high quality research. She is an elected Fellow of the Australian Academy of Science and the Australian Academy of Health and Medical Science. In 2018 Maria was awarded the Alexander Leaf Distinguished Scientist Award for Lifetime Achievement by the International Society for the Study of Fatty Acids and Lipids (ISSFAL).*

## **Beyond the Usual Subjects: The health and developmental implications of the “other” fatty acids in infant nutrition, including arachidonic (ARA) and docosapentaenoic (DPA) acids**

**Douglas Bibus, MSc, PhD**

University of Minnesota, Minneapolis, MN, USA and Lipid Technologies LLC, Austin, MN, USA

Seen from the preceding presentations, the traditional focus of fatty acids, especially in the context of human milk, has directed at long-chain polyunsaturated fatty acids (LC-PUFAs), especially of the  $\omega$ 3 series: docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) with obvious contributions to infant health and nutrition. The evidence for implications of two additional LC-PUFAs, arachidonic acid (ARA, 20:4 $\omega$ 6) and docosapentaenoic acid (DPA, 22:5 $\omega$ 3), for infants is less widely known, but merits recognition as the total profile of human milk fatty acids becomes more accessible to clinicians and investigators. ARA comes from animal-source foods in the diet and can be synthesized endogenously by elongation of linoleic acid. Its involvement in membranes of the CNS implies a role in cognitive development. The derivative eicosanoid series modulates immunity of tolerance and allergy on the T-helper2 domain. ARA is the precursor of endocannabinoids, felt to enhance the sucking and feeding performance of infants (Gaitán et al, 2017). Koletzko (2014), reporting for the Early Nutrition Academy, has suggested a daily intake of ARA of 140 mg/d in formula-fed, full-term infants. The interplay and inter-conversion of DPA with EPA and DHA remains a theme of contention (Metherel et al, 2019). DPA exists at nearly similar concentrations as DHA in breast milk from North American mothers. DPA may play a significant role in supporting DHA and omega 3 status of developing infants and children. With many other FAs over a carbon-length of C18 or longer, the theme of FA:FA interactions is worthy of addressing in maternal milk.

*Douglas Bibus, PhD is a research scientist at The University of Minnesota and operates Lipid Technologies, LLC., an analytical and consulting group that focuses on fatty acid and lipid analysis and integration of lipids in medicine, biotech and food applications. Dr. Bibus’s research interests include the role of essential fatty acids in human and animal nutrition. Dr. Bibus holds a Bachelor of Science degree from Mankato State University, a Master of Science degree in nutrition from the University of Minnesota, and a doctorate in nutritional biochemistry from the University of Minnesota.*

