Milk and Milk Products in Human Nutrition
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Editors
Roger A. Clemens, Los Angeles, CA, USA
Olle Hernell, Umeå, Sweden
Kim Fleischer Michaelsen, Copenhagen, Denmark
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Preface

Milk is the sole source of nutrition for mammals for a period from several days to a few years, depending on species. The complex biology of mammalian milks impacts early growth and development, and may provide a foundation for health throughout the entire lifespan.

Human milk is aimed at being the sole source of nutrition in early infancy, but if breastfeeding is not possible milk substitutes, in general based on cow’s milk protein, need to have a composition fulfilling the same goal of serving as the sole source of nutrition during the first months of life and confer as close as possible the overall health benefits that human milk provides to the infant.

In many populations, milk continues to play a major role in a healthy, balanced diet throughout life. During childhood, pregnancy and adulthood, intake of cow’s milk has important beneficial effects on linear growth, bone development and oral health. Cow’s milk has been especially effective in prevention and treatment of undernutrition in low-income countries. Potentially adverse effects of cow’s milk intake, like increased risk for type 1 diabetes and certain cancers, or negative aspects of dairy fats continue to be under debate in the absence of convincing evidence.

The workshop covered three sessions with excellent presentations of invited lecturers and vivid discussions typical for the Nestlé Nutrition Institute workshops. The first session covered Milk during Pregnancy and Infancy, the second session Milk during Childhood in Low- and High-Income Countries, and the last session General Aspects of Milk: Milk in Adult Nutrition. Together, the three sessions covered most aspects of milk during the life cycle in a global perspective.

This publication includes all the presentations together with the discussions following each of them. The concluding remarks provide a short summary and conclusions drawn from the deliberations of the workshop.

Roger A. Clemens
Olle Hernell
Kim Fleischer Michaelsen
Foreword

Following the workshop on the ‘Biology of Human Milk’ held in 1988, the present 67th workshop was the first one focusing on the health aspects of milk during and beyond the breast milk feeding period, reflecting the major role that milk plays in a healthy, balanced diet across the lifespan. Breast milk is unique, and in the ideal situation, is the sole source of nutrition in early infancy. Breast milk substitutes therefore have to be chosen carefully depending on their suitability for the infant. However, since 1988 the scientific world has reached the consensus that the performance of the breastfed infant rather than the composition of human milk should be the reference for the innovation of breast milk substitutes. The benefits of milk in the diet during the weaning and toddler periods were debated in this workshop, as well as the benefits for school age children and throughout adolescence and adult life. The benefits may be different at different ages.

Amongst the most important beneficial effects summarized during the workshop were:

- Milk remains an important source of dietary calcium, protein, energy, vitamins, minerals, growth factors and other bioactive components in both, low- and high-income countries. Milk can also make a contribution to dietary vitamin D intake, especially when fortified.
- Milk is a crucial part of the diet for child growth and development. There is a clear association with linear growth, although the mechanisms are yet to be fully elucidated.
- Dairy fats contain a range of lipids that may have health-promoting properties including omega-3 LC-PUFA, gangliosides, sphingolipids, etc.

Impact of ingestion of trans-fatty acids or selected saturated fatty acids on health and the association of risk for type 1 diabetes and milk intake were discussed in a balanced manner.

This workshop, held in Marrakech, Morroco, in March 2010, brought together an outstanding group of scientific experts in the field and participants from 30 countries who contributed largely to the lively and intense discussions.
We want to thank the three chairpersons, Prof. Roger Clemens from the USA, Prof. Olle Hernell from Sweden and Prof. Kim Fleischer Michaelsen from Denmark, all highly respected experts in the field of pediatric nutrition, for putting together this outstanding scientific program.

Our special thanks go to Mr. Badr Nassili and Ms. Sophia Jalal and their Nestlé Maghreb team in Morocco for their efficient logistic support and for hosting this workshop in the beautiful environment of Marrakech.

Prof. Ferdinand Haschke, MD, PhD
Chairman
Nestlé Nutrition Institute
Vevey, Switzerland

Dr. Petra Klassen, PhD
Scientific Advisor
Nestlé Nutrition Institute
Vevey, Switzerland
67th Nestlé Nutrition Institute Workshop
Pediatric Program
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Contributors

Chairpersons & Speakers

Prof. Lindsay H. Allen
USDA ARS Western Human Nutrition Research Center
430 West Health Sciences Drive
University of California
Davis, CA 91656
USA
E-Mail lindsay.allen@ars.usda.gov

Prof. G. Harvey Anderson
Department of Nutritional Sciences
University of Toronto
150 College Street
Toronto, ON M5S 3E2
Canada
E-Mail Harvey.anderson@utoronto.ca

Prof. Roger A. Clemens
USC School of Pharmacy
1540 Alcazar Street, CHP G32
Los Angeles, CA 90089
USA
E-Mail clemens@usc.edu

Prof. Robert A. Gibson
Nutrition and Functional Food Science
The University of Adelaide
School of Agriculture, Food & Wine
Waite Campus, Waite Road
Glen Osmond, SA 5064
Australia
E-Mail robert.gibson@adelaide.edu.au

Prof. Olle Hernell
Pediatrics
Department of Clinical Sciences
Umeå University
SE–90185 Umeå
Sweden
E-Mail olle.hernell@pediatri.umu.se

Prof. Ingegerd Johansson
Department of Odontology
Umeå University
SE–90185 Umeå
Sweden
E-Mail Ingegerd.johansson@odont.umu.se

Prof. Bo Lönnervedal
Department of Nutrition
University of California
One Shield Avenue
Davis, CA 95616
USA
E-Mail blonnerdal@ucdavis.edu

Prof. Richard M. Martin
School of Social and Community Medicine
University of Bristol
Canynge Hall
39 Whatley Road
Bristol, BS8 2PS
UK
E-Mail Richard.martin@bristol.ac.uk

Prof. Bodo C. Melnik
Department of Dermatology
Environmental Medicine and Health Theory
Sedanstrasse 115
University of Osnabrück
DE–49090 Osnabrück
Germany
E-Mail Melnik@t-online.de
Contributors

Prof. Kim Fleischer Michaelsen
Department of Human Nutrition
Faculty of Life Sciences
University of Copenhagen
Rolighedsvej 30
DK–1958 Frederiksberg C
Denmark
E-Mail kfm@life.ku.dk

Prof. Christian Mølgaard
Department of Human Nutrition
Faculty of Life Sciences
University of Copenhagen
Rolighedsvej 30
DK–1958 Frederiksberg C
Denmark
E-Mail cm@life.ku.dk

Prof. Ann Prentice
MRC Human Nutrition Research
Elsie Widdowson Laboratory
Fulbourn Road
Cambridge CB1 9NL
UK
E-Mail ann.prentice@mrc-hnr.cam.ac.uk

Prof. Cheryl L. Rock
University of California, San Diego
Department of Family and Preventive Medicine
Moores UCSD Cancer Center
3855 Health Sciences Drive
La Jolla, CA 92093-0901
USA
E-Mail clrock@ucsd.edu

Prof. Dennis Savaiano
Department of Foods and Nutrition
Purdue University
Room 1G-G Stone Hall
West Lafayette, IN 47907
USA
E-Mail savaiano@purdue.edu

Prof. Inga Thorsdottir
Unit for Nutrition Research
Faculty of Food Science and Nutrition
School of Health Sciences
University of Iceland and University Hospital
IS–101 Reykjavik
Iceland
E-Mail ingathor@landspitali.is

Prof. Rachida Boukari
University Pediatric Hospital
Blida
Algeria
E-Mail rachida_boukari@yahoo.fr

Prof. Fatima Dehbi
Pediatric Hospital Ibn Rochd
Casablanca
Morocco
E-Mail dehbi_fatima@yahoo.fr

Prof. Nezha Mouane
University Pediatric Hospital Ibn Sina
10001 Rabat
Morocco
E-Mail nmouane@medprof.co.za

Invited Attendees

Mohamed Tahar Hamlaoui/Algeria
Chawki Ahmed Kaddache/Algeria
Maria Makrides/Australia
Tahmina Begum/Bangladesh
Fazlul Haque/Bangladesh
Mohammed Sarwar Ferdaus/Bangladesh

Martin Ondoa Mekongo/Cameroon
Mohamed Elbarbary/Egypt
Ahmed Elhawawy/Egypt
Hugues Piloquet/France
Carl Peter Bauer/Germany
Nana Kweku Okai Brako/Ghana
Contributors

Pierre Detry/France
Yong Kim Lacoste/France
Jorge Ottoniel Palacios
Rosales/Guatemala
Bavdekar Ashish/India
Anjan Bhattacharya/India
Pankaj Garg/India
Parameswarappa Haralappa/India
Vinay Hanamesh Joshi/India
Deeksha Kapur/India
Neelam Mohan/India
Padmanab Reddy Mriddy/India
Valavanur Subramani
Sankaranarayanan/India
Rahul Jagdishlal Verma/India
Giovanni Corsello/Italy
Berthe Evelyne Lasme-Guillao/Ivory Coast
Peter Ngwatu/Kenya
Roger Adrianasolo/Madagascar
Moises Gerardo del Hoyo/Mexico
Lourdes Lemus/Mexico
Asmaa Alaoui Mdaghri/Morocco

Said Benomar/Morocco
Rachida Chami/Morocco
Pedro Alinia/Mozambique
Seline Okolo/Nigeria
Julia Deleon/Philippines
Marysia Recto/Philippines
Rute Neves/Portugal
Paulo Oom/Portugal
Joana Saldanha/Portugal
Elena Lukushkina/Russia
Fahad Alaql/Saudi Arabia
Ibrahim Alhifzi/Saudi Arabia
Mashudu Manafe/South Africa
Ingrid Schoeman/South Africa
Leigh-Ann Silber/South Africa
Christian Brägger/Switzerland
Abdul Wahab Chami/Syria
Sungkom Jongpiputvanich/Thailand
Samir Boukthir/Tunisia
Abdelaziz Harbi/Tunisia
Naima Khrouf/Tunisia
Zahra Marrakchi/Tunisia
Mary Fewtrell/UK

Nestlé Participants

Pierre Detry/France
Yong Kim Lacoste/France
Mike Possner/Germany
Serge Dzeukou/Ghana
Panagniotis Bagkas/Greece
Sanjeev Ganguly/India
Linda Belached/Morocco
Olivier Desponts/Morocco
Moungi Elmernissi/Morocco
Samia Hachami/Morocco
Sophia Jalal/Morocco
Badr Nassili/Morocco
Thomas Wettstein/Morocco

Charisses Dilla/Philippines
Catarina Durao/Portugal
Olga Netrebenko/Russia
Anne-Marie de Beer/South Africa
Stefan Bodenstab/Switzerland
Anne Marie Braunius/Switzerland
Ferdinand Haschke/Switzerland
Petra Klassen Wigger/Switzerland
Sophie Pecquet/Switzerland
Florence Rochat/Switzerland
Magali Thieulent/Switzerland
Sabine von Manteuffel/Switzerland
Concluding Remarks

It is our privilege to summarize the workshop and to make some concluding remarks. Let us begin by thanking the speakers for their excellent contributions and all participants for actively participating in the discussions.

The first session started with Ann Prentice who addressed the effects on maternal, fetal and infant bone of milk, calcium and vitamin D intake during pregnancy and lactation. Despite the transfer from mother to infant of 200–300 mg calcium/day during the last trimester of pregnancy and during breast-feeding, physiological changes during these conditions are independent of maternal calcium intake. Neither are increases in maternal calcium intake necessary, nor are they effective in reducing maternal losses. There is no evidence of an increase in biological requirement of vitamin D during pregnancy, but many mothers and infants do have hypovitaminosis D (defined as a plasma concentration of 25OHD below 25 nm, or 10 ng/ml), with increased risk of clinical vitamin D deficiency including rickets and osteomalacia. Vitamin D deficiency in the mother during pregnancy is associated with vitamin D deficiency in the newborn infant with its many sequelae. Safe sun exposure and dietary supplementation are effective and should be promoted for all pregnant and lactating mothers as a measure to reduce these risks.

Next, I spoke on the differences between bovine and human milk and the evolution of infant formulas. Not only does each species have a unique composition of its milk reflecting the specific needs of its offspring, but the composition varies also within a species, and an individual. The goal to minimize the difference in performance between breastfed and formula-fed infants will drive future development of infant formulas. Some of the many bioactive milk components are attractive ingredients in future formulas to achieve that goal. However, some of them have species-specific activities and others are truly species specific as milk components. The bile salt-stimulated lipase in human milk, which compensates for low endogenous capacity to digest dietary fat in the newborn, is absent from bovine milk but can now be produced by recombinant techniques in quantities making it possible for supplementation.
of formulas. With novel ingredients, some with potent biological activities, produced with new techniques, it will be extremely important to rigorously evaluate and document safety and efficacy. All improvements may not be worth a higher cost – ‘functional effects’ are not necessarily the same as beneficial health effects.

*Inga Thorsdottir* pointed out that one of the major reasons for refraining from consumption of whole cow’s milk in infancy is the risk for iron deficiency anemia and its consequences. Other potential risks relate to the high renal solute load, of particular concern to infants and children suffering from dehydration. A population-based infant cohort study in Iceland, carried out in 1995–1997 when the tradition was to wean infants from the breast to whole cow’s milk, showed that low iron status at 12 months of age was indeed strongly associated with whole cow’s milk intake at 9 and 12 months of age, and a follow-up at 6 years revealed an increased risk of overweight among boys who had higher protein and milk intake in infancy, and iron deficiency in infancy was associated with lower developmental scores at 6 years. A second cohort study conducted between 2005 and 2007, when new national public health recommendations, including use of follow-on formula rather than whole cow’s milk had been adopted, showed improved iron status.

*Bo Lönnerdal* spoke on biological effects of novel bovine milk fractions. Besides its ideal amino acid composition, α-lactalbumin, which is the dominant human whey protein, seems to have several functions. The iron-binding protein lactoferrin is an even better example of a milk protein with several biological activities, both in its native and partly digested forms. Some effects have been disputed, and the lack of evidence in some earlier studies may have been due to contamination by lipopolysaccharide of commercial bovine lactoferrin fractions. Osteopontin is a possible key molecule in the induction of Th1 responses and may stimulate the postnatal Th1/Th2 switching, but also affects bone mineralization and growth. Osteopontin binds lactoferrin and some effects of lactoferrin may in fact be facilitated by osteopontin. A novel bovine milk fraction is enriched in milk fat globule membrane, which contains a number of proteins, e.g. lactadherin, butyrophilin, xantine oxidase and mucin with antimicrobial effects in vitro, and lipids e.g. sphingomyelin and gangliosides which may affect signal transduction and neurodevelopment. This fraction has been low in formulas, but it is now available as a possible ingredient and its potential effects are evaluated in clinical studies.

Finally, *Ingegerd Johansson* mentioned that breastfed infants differ distinctly from non-breastfed infants in their composition of the oral microbiota. Breastfeeding might promote a health-associated microbiota in the dental biofilm, which is unique compared to other compartments of the digestive tract, and hinder establishment of cariogenic mutans streptococci. Focus has shifted from specific cariogenic bacteria to the composition of the eco system of this biofilm, as an important factor in caries development. Non-sweetened dairy products, in particular caseins and casein-derived peptides, which are
proven non-cariogenic, or specific bioactive components derived from such products might prove to be part of future preventive strategies against caries. For instance, studies in children have shown that consumption of milk or hard cheese is associated with less caries. However, although in vitro and observational studies are promising, randomized clinical trials are needed to reveal if dairy products could indeed be a future cost-effective complementary treatment to proper oral hygiene, sugar restriction and use of fluoride for oral health.

Olle Hernell

The second session was on milk during childhood in low- and high-income countries.

First Christian Mølgaard talked about milk and linear growth. There is strong evidence that milk stimulates linear growth both from observational and intervention studies in low-income countries, but also observational studies and a few intervention studies in industrialized countries suggest an effect. The mechanism is not clear. It is quite obvious that IGF-I and perhaps insulin play an essential role, but it is not known which components in milk stimulate growth. More research, especially with long-term follow-up of intervention studies, is needed to better understand this, which was also recommended by Richard Martin. Whey and/or casein seem to have a positive effect on lean body mass, but whether it is also the case in malnourished children is not clear. The long-term consequences of the effects of milk on linear growth are most likely mixed with both positive and negative effects.

Then, Richard Martin talked about the role of milk in programming of the IGF-I axis and which implications this can have for health in adulthood. He presented evidence that milk intake is positively associated with higher levels of circulating IGF-I in children and adults and that higher circulating IGF-I promotes linear growth in children, but also that milk intake in early life is inversely associated with IGF-I levels in adult life. Thus, there seems to be a long-term programming of the IGF-I axis, with high milk intake early in life being associated with lower IGF-I levels as adults, which could have implications for risk of cancer and ischemic heart disease later in life.

IGF-I was also a theme in the presentation given by Bodo Melnik. As a dermatologist, he has studied the epidemiology of acne vulgaris, which is the most common skin disease in industrialized countries. He suggested that milk, especially whey, plays a central role in acne pathogenesis through stimulation of IGF-I and insulin. The epidemic of acne is most likely the visible metabolic syndrome of skin caused by an exaggerated insulinotropic diet, which also includes high intake of carbohydrates, he said. If milk intake and thereby stimulation of IGF-I and insulin is reduced, he suggested that this would reduce the incidence of obesity, diabetes mellitus, cancer, neurodegenerative disease and acne. However, the available epidemiological data on milk
intake and lifestyle diseases do not support this view, as presented in several of the talks in the third session of this meeting.

*Lindsay Allen* talked about the effects of animal source foods in low-income countries with emphasis on milk. Many observational studies show positive associations between intake of animal source foods and better growth, cognitive and motor development and physical activity, but there are only few intervention studies available. These showed that milk had a positive effect on height and weight, especially in the younger children, and meat improved cognitive function and physical activity. Some of these effects could be caused by the high content of vitamin B12 in animal source foods.

I talked about the role of cow’s milk in the treatment of moderate and severe malnutrition. The development of products to treat severe acute undernutrition, F100 and RUTFs, have reduced mortality and increased weight gain considerably, and part of the success is likely to be due to the high content of milk in these products. The beneficial effects are most likely due to the high content of bioavailable proteins and minerals and because there are no fibers and antinutrients as in plant-based foods. Furthermore, the high lactose content might add beneficial effects. Milk-based products would also be beneficial for the many millions of children with moderate undernutrition, but milk-based products are expensive. Therefore, one strategy is to add small amounts of milk powder to cereal-based fortified blended foods, but there is a need for randomized controlled trials to determine the amount of milk protein that has the optimal cost effectiveness in treating moderate undernutrition.

*Kim Fleischer Michaelsen*

I would like to extend my appreciation to *Harvey Anderson, Robert Gibson, Cheryl Rock* and *Dennis Savaiano* for their contribution to this wonderful session with Nestlé.

The preponderance of evidence indicates milk proteins can affect a reduction in food intake, lower postprandial blood glucose, with a concomitant increase in blood insulin concentration. These effects suggest that the consumption of dairy products may be important in bodyweight management and reducing comorbidities of metabolic syndrome. Even those with a self-report history of lactose intolerance may benefit since the more typical response following milk intake is symptoms of maldigestion. Thus, even among mal-digesters who have a limited ability to digest lactose, dairy products can provide a spectrum of essential nutrients for growth and development. Equally important, epidemiological evidence suggests milk-derived nutrients, such as calcium, may reduce the risk of colorectal cancer, possibly increase the risk of prostate cancer, while the impact of calcium on other cancers, such as breast and ovarian, is mixed or lacking. Similarly, the association of milk proteins with the risk of type 1 diabetes is inconsistent, although dairy fats, including saturates and omega-3 fatty acids, may be cardioprotective.
Concluding Remarks

dence indicates that stearic acid, a saturate, and that the naturally occurring trans fatty acids, such as conjugated linoleic acid, are nonatherogenic. Collectively, many components of milk can provide health benefits beyond normal growth and development.

Roger A. Clemens

It’s time to close the scientific part of this workshop. I must say, it turned out as we expected, more questions have been raised than answers have been provided, and I think it’s good that we are in a continuous discussion and that we are critical. We are challenging paradigms and are moving to the next step.

I said 10 years ago in a workshop that perhaps full fat milk is not bad for your health if you consume it long-term. Today, a lot of people would criticize me for this and would say that we promote industry products. Today, I think the opinion that was expressed by both, also by the committee, is a little bit different, so we can be happy that dairy products, which play a major role in our lives, are good for our long-term health. Still, I have been in my job for some decades now, and I must tell you that whatever you say the probability of it being wrong 10 years later is 50%, so there is always time for a new workshop in 10 years to review what we have said today and move forward.

This brings me to thank the three chairmen of this workshop; they have been working with us since June last year, and I think they have brought together a very good comprehensive program; it was not easy because we were combining fetal life with early infancy, poor countries and the long-term outcome of health effects.

I want to thank the three moderators, Nezha Mouane, Fatima Dehbi and Rachida Boukari. I think they did their job in a very charming way, and even when it was not so clear who was raising the hand at the back, I think most of the people who wanted to speak could speak up. The discussion in my opinion always contributes significantly to the outcome and to the content of the workshop.

This workshop would not have been possible without the support of local organization and I would like to thank Sophie and Samir. Last but not least Petra, I think she did a great job, thank you.

Ferdinand Haschke
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