Early Nutrition: Impact on Short- and Long-Term Health

Nestlé Nutrition Institute Workshop Series
Pediatric Program, Vol. 68

Early Nutrition: Impact on Short- and Long-Term Health

Editors
Hans van Goudoever, Amsterdam, The Netherlands
Stefano Guandalini, Chicago, IL, USA
Ronald E. Kleinman, Boston, MA, USA

KARGER

Nestlé Nutrition Institute

Nestec Ltd., 55 Avenue Nestlé, CH–1800 Vevey (Switzerland)
S. Karger AG, P.O. Box, CH–4009 Basel (Switzerland) www.karger.com

Printed in Switzerland on acid-free and non-aging paper (ISO 9706) by Reinhardt Druck, Basel
ISBN 978–3–8055–9745–6
e-ISBN 978–3–8055–9746–3
ISSN 1661–6677

Library of Congress Cataloging-in-Publication Data

Nestlé Nutrition Workshop (68th : 2010 : Washington, D.C.)
Early nutrition : impact on short- and long-term health / editors, Hans van Goudoever, Stefano Guandalini, and Ron Kleinman.
p. ; cm. -- (Nestlé Nutrition Institute workshop series pediatric program, ISSN 1661-6677 ; v. 68)
Includes bibliographical references and index.
ISBN 978-3-8055-9745-6 (alk. paper) -- ISBN 978-3-8055-9746-3 (e-ISBN)
I. Goudoever, Hans van. II. Guandalini, Stefano. III. Kleinman, Ronald E. IV. Title. V. Series: Nestlé Nutrition workshop series. Paediatric programme ; v. 68. 1661-6677
[DNLM: 1. Infant Nutritional Physiological Phenomena--Congresses. 2. Child Nutritional Physiological Phenomena--Congresses. 3. Feeding Behavior--Congresses. 4. Prenatal Nutritional Physiological Phenomena--Congresses. W1 NE228D v.68 2011 / WS 120]
LCclassification not assinged
613.2'69--dc23

2011028522

KARGER

Basel · Freiburg · Paris · London · New York · New Delhi · Bangkok · Beijing · Tokyo · Kuala Lumpur · Singapore · Sydney

Contents

Preface

Over the past decade, major advances have occurred in our understanding of the interaction of genetics and environment (and particularly diet) in health and disease. Thus, it is very germane now to have a workshop dedicated to a review of nutritional practices and feeding behaviors in infancy and early childhood since these not only have a significant influence on the immediate growth and health of the child, but potentially affect long-term health issues such as obesity and hypertension, which often have antecedents early in life. This volume presents the proceedings of the 68th Nestlé Nutrition Workshop held in October 2010 in Washington, DC. The chapters in this book are organized, like the workshop, in a progression from the newborn period to childhood. They are the work of a selected group of international experts in infant and childhood nutrition, and represent the latest knowledge regarding feeding practices during this time and how those impact growth, development and immediate and long-term health.

A significant body of research has demonstrated a major impact of maternal nutrition during fetal life on later health and development of the newborn. This formed the basis of a robust discussion in the first session of the symposium, and draws our attention to the potential long-term effects of specific macronutrients and micronutrients in the maternal diet during human fetal development. One example of this is the recent data on the impact of dietary lipid components as well as proteins in the maternal diet during fetal and early newborn life on various functional outcomes in the developing infant and child. These data are now informing our feeding practices in the newborn critical care unit, particularly with regard to the use of human donor milk and the use of probiotics in the diet of premature and ill newborns. The use of probiotics in this context still poses challenges, since we can clearly influence the gut microbiome to some extent, but the specific microorganisms that should be used, the dose and administration schedule remain subject to significant debate. Thus, this area of fetal and newborn nutrition and its influence on later health is a vibrant and active subject of discussion and investigation, and holds promise for important discoveries on the role of early

nutritional interventions in both short- and long-term health and development.

It is clear from the results of recent surveys presented in the second session of the symposium that in both the developed as well the developing world, even in countries with vibrant economies, a significant number of infants and young children are not consuming the types of foods that have been recommended to support optimal health. As a consequence, an insufficient intake of selected micronutrients, such as iron and zinc, is highly prevalent, particularly in the developing world. A unique and very successful approach using coated micronutrients for supplementing the diets of vulnerable children to address this serious threat to both immediate and long-term health and development is described in this section of the book. Taste perception plays an extremely important role in food preferences. With the current emphasis on reducing the intake of salt and sugars in the diet, the discussion of the science of taste perception and in particular how it develops during gestation, infancy and early childhood contributed significantly to the overall dialogue on nutritional support during this period. In addition to availability, affordability, taste and cultural preferences, the increasing prevalence of allergic reactions to foods during this time of life often determine the types of foods offered. The discussion of the basis and evolution of immunologic reactions to foods in early life was highly informative to the overall dialogue, and provided the basis for further discussion in the next session which focused on the consequences of weaning and subsequent feeding practices on health during late adolescence and adulthood.

The final session of the workshop spanned diverse areas, and major updates were provided on topics that have seen exciting developments in the recent years. Participants could appreciate new – and in some ways revolutionary – information on the influence of early feeding practices on the later development of a number of health-related issues such as food allergies, later food preferences and eating habits, obesity, bone development, the risk of developing celiac disease in genetically predisposed children, and even – albeit at the moment mostly from studies in animals – on longevity! The microbiome and its influence on growth, weight gain and immediate and long-term health are an emerging area of biology that led to a particularly lively discussion. As always, the discussion provided by those who attended the meeting proved exceptionally interesting and informative.

As the Chairs of this workshop, we are particularly indebted to Prof. Ferdinand Haschke and his colleagues at the Nestlé Nutrition Institute. They provided a format and setting that proved to be perfect for engagement, discussion and learning. On behalf of all those who participated in this workshop, we thank you.

Hans van Goudoever
Stefano Guandalini
Ronald E. Kleinman

Foreword

The 68th Nestlé Nutrition Institute Workshop was dedicated to a research area that is gathering a significant amount of interest in the scientific arena: Early nutrition and its impact on long-term health. The International Society for Developmental Origins of Health and Disease has only recently released a position paper on the importance of nutrition in the first 1,000 days [World Nutr 2011;2:195–205].

The scientific evidence from animal and human data showing effects of early nutrition on later health were presented by a group of renowned experts in the field and discussed by an international audience of outstanding health professionals. The topics covered ranged from the nutrition of preterm infants including suggestions on how to improve their short-term outcome by not comprising long-term health, to an evaluation of the current feeding habits of toddlers in different parts of the world. Both problematics, that of 'over'-feeding and 'under'-feeding and related malnutrition, were discussed with respect to their long-term outcome. Both weigh equally in their public health burden.

This excellent scientific program was brought together by the three chairpersons, Prof. Hans van Goudoever, Prof. Stefano Guandalini and Prof. Ron Kleinman, to whom we address our special thanks. All three are highly respected in the field of nutrition.

Special thanks go also to Linda Hsieh and her team from the US for her excellent organization and hosting in Washington.

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

Dr. Petra Klassen, PhD
Scientific Advisor
Nestlé Nutrition Institute
Vevey, Switzerland

68th Nestlé Nutrition Institute Workshop
Pediatric Program
Washington, DC, October 17–21, 2010

Contributors

Chairpersons & Speakers

Prof. K.N. Agarwal
President Healthcare and Research Association for Adolescents
D-115, Sector-36, NOIDA
New Delhi 201301
India
E-Mail: adolcare@hotmail.com

Prof. Alexander Baturin
Institute of Nutrition RAMS
Kashirskoe av 21
Moscow
Russia
E-Mail: baturin@ion.ru

Prof. Leann L. Birch
Center for Childhood Obesity Research
129 Noll Laboratory
The Pennsylvania State University
University Park, PA 16802
USA
E-Mail: llb15@psu.edu

Prof. Alessio Fasano
Mucosal Biology Research Center and Center for Celiac Research
University of Maryland School of Medicine
Health Science Facility II, Room S345
20 Penn Street
Baltimore, MD 21201
USA
E-Mail: afasano@mbrc.umaryland.edu

Prof. Stefano Guandalini
Section of Pediatric Gastroenterology
University of Chicago
Comer Children's Hospital
5721 S. Maryland Avenue
Chicago, IL 60637
USA
E-Mail: sguandalini@peds.bsd.uchicago.edu

Prof. Jane Harding
The University of Auckland
Private Bag 92019
Auckland Mail Centre
Auckland 1142
New Zealand
E-Mail: j.harding@auckland.ac.nz

Prof. Martin Holzenberger
Research Center St-Antoine
INSERM - UPMC, UMR S 938
Faculté de Médecine Pierre et Marie Curie
11 étage, porte 1109
27 rue Chaligny
FR–75571 Paris 12
France
E-Mail: martin.holzenberger@inserm.fr

Prof. Sheila Innis
Child & Family Research Institute
Nutrition & Metabolism Research Program
Division of Neonatology
Department of Pediatrics
950 West 28th Avenue
Vancouver, BC V5Z 4H4
Canada
E-Mail: sinnis@interchange.ubc.ca

Prof. Graeme Jones
Menzies Research Institute
17 Liverpool Street
Hobart TAS 7000
Australia
E-Mail: g.jones@utas.edu.au

Prof. Ronald E. Kleinman
Massachusetts General Hospital
CPZS 578
175 Cambridge Street, Suite 578
Boston, MA 02114
USA
E-Mail: rkleinman@partners.org

Prof. Gideon Lack
Children's Allergies Department
2nd Floor South Wing
St Thomas' Hospital
Westminster Bridge Road
London SE1 7EH
UK
E-Mail: gideon.lack@kcl.ac.uk

Prof. Julie Mennella
Monell Chemical Senses Center
3500 Market Street
Philadelphia, PA 19104-3308
USA
E-Mail: mennella@monell.org

Prof. Wayne Shreffler
Massachusetts General Hospital
Center for Immunology and
Inflammatory Diseases
Bldg. 149, 13th Street, Room 8.312
Charlestown, MA 02129
USA
E-Mail: wshreffler@partners.org

Prof. Anna Maria Siega-Riz
The University of North Carolina at
Chapel Hill
Department of Nutrition
Chapel Hill, NC 27599
USA
E-Mail: am_siegariz@unc.edu

Prof. Karen Simmer
School of Women's and Infant Health
University of Western Australia
35 Stirling Highway
Crawley, WA 6009
Australia
E-Mail: Karen.simmer@uwa.edu.au

Prof. Nicolas Stettler
University of Pennsylvania
The Children's Hospital of
Philadelphia
CHOP North 1559
34th Street and Civic Center Blvd
Philadelphia, PA 19104-4399
USA
E-Mail: nstettle@upenn.edu

Prof. Hania Szajewska
The Medical University of Warsaw
Department of Pediatrics
Działdowska 1
PL–01-184 Warsaw
Poland
E-Mail: hania@ipgate.pl

Prof. Hans van Goudoever
Emma Children's Hospital/AMC
Room H7-276
Meibergdreef 9
PO Box 22660
NL–1100 DD Amsterdam
The Netherlands
E-Mail: h.vangoudoever@amc.uva.nl

Prof. Stanley Zlotkin
The Hospital for Sick Children
555 University Avenue
Toronto, ON M5G 1X8
Canada
E-Mail: stanley.zlotkin@sickkids.ca

Moderators

Prof. William Klish
Baylor College of Medicine
Houston, TX
USA
wjklish@hotmail.com

Dr. Jose M. Saavedra
Nestlé Nutrition
North America
jose.saavedra@us.nestle.com

Prof. Alan Lake
The John Hopkins University
School of Medicine
Baltimore, MD
USA
alakeslake@aol.com

Invited Attendees

Peter Fryer/Australia
Sam Mehr/Australia
Manzoor Hussain/Bangladesh
Sirajul Islam/Bangladesh
Saifur Rahman/Bangladesh
Cristina Jacob/Brazil
Clea Leone/Brazil
Peirre-Fernand Tchokoteu/Cameroon
Mark Kovacs/Canada
Andrea Papamandjaris/Canada
Qi Feng/China
Jorge Andres Chacón Rey/Colombia
Patricia Contreras/Colombia
Wilson Daza Carreño/Colombia
Maria Elena Giraldo/Colombia
Julian Grajales Rojas/Colombia
Diana Mora/Colombia
Victoria Eugenia Morales Rojas/Colombia
Maria Cristina Noreña Velásquez/Colombia
Maria Elena Venegas/Colombia
Miguel Viaña/Colombia
Charlotte Casper/France
Frederic Gottrand/France
Yong Un Kim Lacoste/France
Alexandra Papadopoulou/Greece
Aglaia Zellou/Greece
Jose Fernando Menendez/Guatemala
Ravindra Chittal/India
Rajeshwar Dayal/India
Sanjeev Ganguly/India
Apurba Ghosh/India
Kartik Nagesh/India
Seema Puri/India
Satish Saluja/India
Arun Singh/India
Umesh Vidyadhar Vaidya/India
Asril Aminullah/Indonesia
Dedet Hidayati/Indonesia
Fredrick Were/Kenya
Sergio Fernández/Mexico
Marycruz García/Mexico
Luis Manuel González/Mexico
María Victoria Lima/Mexico
Armando Madrazo/Mexico
Reynaldo Michel/Mexico
Victor Uscanga/Mexico
Salvador Villalpando/Mexico
Edmond Rings/Netherlands
Marjan Skotnicki-Hoogland/Netherlands
Ruurd van Elburg/Netherlands
Jose Salazar/Philippines
Grace Uy/Philippines
Anna Rybak/Poland
Luís Pereira-da-Silva/Portugal
Natalya Vagemans/Russia
Marco Turini/Singapore
Goqwana Bevan/South Africa
Anne-Marie De Beer/South Africa
Trish Hall/South Africa
Inger Öhlund/Sweden
Ferdinand Haschke/Switzerland
Petra Klassen Wigger/Switzerland
Martinas Kuslys/Switzerland
Laurence Stoll-Le Guyader/Switzerland
Sze Tan/Switzerland
Pramote Praisuwanna/Thailand
Daniel Tumwine/Uganda
Nicola Bradley/UK
Rachel Adams/USA
Lillian Beard/USA

Jami Boccella/USA
Pamela Cekola/USA
Denise Deming/USA
Jo Ann Hattner/USA
Aimee Henrikson/USA
Linda Hsieh/USA
Kathleen Novak/USA
Kathleen Reidy/USA
Carol Siegel/USA
Heidi Storm/USA
Terri Voss/USA
Vinod Kumar Pandey/Zambia

van Goudoever H, Guandalini S, Kleinman RE (eds): Early Nutrition: Impact on Short- and Long-Term Health.
Nestlé Nutr Inst Workshop Ser Pediatr Program, vol 68, pp 251–257,
Nestec Ltd., Vevey/S. Karger AG, Basel, © 2011

Concluding Remarks

I would like to thank the audience for their participation in the discussions. We have left a lot of time for questions, and the participants from all continents were very active. The questions raised were very relevant to their own situation. That was wonderful, and I would like to thank *Jose Saavedra* for co-chairing this session, which was great fun.

Jane Harding started with the basics, as she said. She showed us which models are applicable to human research. She stated that animal models are not models for humans, but that one can learn from reactions of different species and find out whether the same can be observed in humans. There is a distinction between fetal and maternal metabolism. Fetal nutrition is directly linked to fetal growth and subsequently postnatal disease risk. Another important lesson I learned is that a change in micronutrient intake before birth has long-term consequences. Weight gain might not be the best marker, and body composition might be better. Some people in the audience actually stressed that point. The effects of different micronutrients, i.e. glycine on blood pressure, taurine on pancreatic function, and calcium (do not give too much, but be aware of effects of undersupplementation as well) also on blood pressure, are striking. The timing of nutritional changes, e.g. periconceptual undernutrition, might result in early deliveries and all kinds of metabolic changes. *Jane Harding* raised a large set of questions which will keep us occupied for a long time.

Elisabeth Novak from Canada gave a marvelous presentation. She showed us the functional role of different fatty acids in different organs. To give you some highlights: the influence of maternal fatty acid status on the fetal status, the influence of omega-3 fatty acids on appetite behavior, increased omega-6 fatty acids and decreased omega-3 fatty acids in our diets, with all the different consequences of that, lower DHA might for instance influence the neuronal migration pattern, which to me as a neonatologist is an important issue. So, thank you very much for sharing your work with us, you did a marvelous job.

I was talking about amino acids and proteins, and I hope I showed you how important early nutrition is on later outcome in premature infants. In premature infants, nutrition can sometimes have direct and sometimes indirect effects on later outcome.

Karen Simmer showed us the knowns and unknowns of human milk banking. Indeed, 20 years ago it was very popular all over the world. In my own experience (setting up a milk bank in the Netherlands), I noticed that many people were raised with donor milk, especially during the last part of World War II. The milk banks were completely shut down during the HIV epidemics, and now they reappear. I congratulate you for the professionalism with which you described the setting up of a milk bank together with the guidelines. You have set the stage basically, and I think that many people around the world will benefit from your effort.

Finally, *Hania Szajewska* talked about systematic reviews addressing the question whether probiotics should be used, and if so, when. It was interesting to see that about 20% of the audience would advise parents to give probiotics to normal-term infants, 50% would do so in preterm infants, and again about 50% would do that in a high-risk population in their own units.

This session was a truly multinational effort to understand the effects of nutrition or supplements, such as probiotics, on later outcome. These effects might be simulated in animals, but in the end human research will help us most in determining effect size. Clearly, effects are different when the nutritional interventions are timed at different developmental stages. Interventions around the time of conception might result in other effects than similar interventions later in life.

Hans van Goudoever

I would like to thank all of the speakers for their most interesting presentations and the discussions that followed. These highlight the paradoxes that confront us with global public health nutrition issues today. Obesity is increasingly prevalent in both developed and developing nations, and yet hunger and food insufficiency remain highly prevalent across the globe in both wealthy and resource-constrained countries. Thus, hunger, malnutrition and obesity co-exist in a single population or country, and understanding the causes becomes extremely important in devising the optimal public health approach.

The 2008 FITS study provides an impressive view of the most recent food consumption data among young children in the US. Fruit and vegetable consumption is pretty clearly not meeting current recommendations. In contrast, breastfeeding duration has increased, although we are still not meeting the millennium goals. We do know from data that weren't presented yesterday that the rate of increase in obesity among 0- to 5-year-olds in the United States seems to have leveled off, which is very encouraging, and as the data

from the FITS study are further analyzed, we may begin to have some insight into the nutritional contribution to those trends.

India, like the US has impressive resources and is a highly developed nation in many ways. As *K.N. Agarwal* pointed out, India is a nation that exports food and is highly food sufficient. Yet, the prevalence of nutrient deficiencies, such as iron deficiency, is astounding. The data on iron deficiency from one of the cohorts that was presented are derived from a population of children living in the neighborhood of a major medical school and medical center. This demonstrates the public health paradox as dramatically as I have ever seen it displayed. In a high-technology environment where food is very available to many, some children continue to be subject to severe nutrient deficiencies. This reinforces that we all need to be engaged in social policy development and promote social policies that will make food available to those who are most in need of it.

Russia, another highly developed nation with advanced technology, reports a fairly small prevalence of hunger but a rising prevalence of obesity, particularly in childhood. There too, however, is an unusually high prevalence of anemia and perhaps other micronutrient deficiencies that were described by *Alexander Baturin*. This again reinforces the need to support not only appropriate social policies but effective programs that can address these nutritional issues.

One approach to addressing micronutrient deficiencies is the program designed and described by *Stanley Zlotkin* that provides 'sprinkles', a microencapsulated supplement that can be sprinkled on food and provides the micronutrients missing from the usual diet in a way that's easy and acceptable to families and children. Thus, this is a culturally acceptable program that is unique and has been shown to be a highly effective way of delivering micronutrients as well as nutrition education to children and families.

The last two presentations of this session addressed the issue of 'sensitivities'. *Julie Mennella* discussed how taste sensation develops over the period of infancy and childhood, and the fact that there seem to be some unique periods of time in life such as early in infancy, when there are opportunities to influence taste perception and the acceptance of specific flavors later on in childhood. The molecular biology of taste perception and the evolution of these pathways during infancy and childhood are extraordinarily interesting and important. We know that taste receptors are present not only in the mouth but in the gut as well. Understanding the physiologic effects of these receptors in the gastrointestinal tract is the subject of significant ongoing research which will enlighten our understanding of satiety and satiation. We also learned that taste perception or preference is perpetuated over time, not only by the exposure to the flavor(s) but by the context in the environment that the tastes are presented. One could conclude that having your mother threatening you with a penalty if you don't consume your vegetables may influence your taste preferences for vegetables in a different way than watch-

ing Sesame Street, seeing Grover eating vegetables, and then being given the vegetables with your lunch and being encouraged pleasantly to eat them.

In the final presentation of the session, we heard about the very complex pathways that lead to immune tolerance and how these evolved over time to downregulate the potential of adverse immune responses to allergens in our diet or in our environment. Thus, the normal progression of immune-mediated responses to potential dietary antigens present in all foods leads to a regulatory process that controls and prevents an adverse immune response. In allergic individuals, the dose of antigen, the timing of exposure during the life cycle (prenatal, postnatal, infancy, childhood, adulthood) and the chemical structure and composition of the putative allergen help to govern whether or not the response develops into a clinical allergic response or if the immune system develops a tolerant response to these antigens so that we are not constantly reacting to various substances in the diet and the environment.

Thus, I've presented a very brief review of the presentations and discussions from this session. I have enjoyed it tremendously, and appreciate all of the work and effort that the speakers gave to their presentations. I particularly appreciated the questions and subsequent discussion that I heard from so many of you in the audience. This has been a great learning experience for me, and I think this kind of interaction between experts from all parts of the globe has so much more significance because of the diverse experiences represented here. I want to extend my thanks to all of you for your participation.

Ronald E. Kleinman

Well, we had a whole day and 6 wonderful lectures and discussions; it is now my difficult task to summarize it all.

Gideon Lack told us about the increased rates of food allergies in children, and this is apparently a worldwide phenomenon. He also told us that the time-honored principle of food allergen avoidance for the first year of life and beyond may no longer hold true. In fact, the latest statements from the UK and even from the USA appear to be now much more doubtful about recommending delayed introduction of potential allergens. On the contrary, there is emerging evidence that having early exposure to allergens might be beneficial if this occurs via the oral route as it might actually lead to tolerance. If the exposure occurs through the skin, especially when the skin is more readily available to increase permeability due to inflammation, this may actually predispose to development of allergies. Therefore, strategies to prevent sensitization might include treating eczema, eliminating the environmental allergens that we heard tend to persist for a long time, and possibly early oral exposure to the allergens. Of course, it won't be until the next 2–3 years when we hear the results of the LEAP and the EAT studies that we will know for sure whether this is really the right way to follow, but so far the evidence seems to be amounting in this direction.

Leann Birch stressed very important findings on the early development of taste in children. Infants and young children are wired to like sweet and salty foods and dislike bitter and sour ones. Such choices were desirable when scarcity of food for prolonged times was commonplace; but now that we live in an 'obesogenic' environment, they are no longer valid. *Leann Birch* showed that we may actually influence our infant's choices very early on by a number of mechanisms, for instance by repeating the exposure to foods initially rejected even for 15 or 20 times so that they become familiar with such tastes and eventually accept them. Several methods can be employed to achieve this familiarization, including presenting new foods with a positive reinforcement like attention from adults or music, etc. The most important message was that the dietary transition that occurs in the first 2 years of life is a period of a tremendous opportunity for primary prevention.

Alessio Fasano told us a number of interesting, exciting things. We learned that there are up to 27 additional genes outside of the HLA region that seem to contribute to the predisposition to celiac disease, and the time might never come when we will have the final complete genetic mapping of the predisposition to celiac disease. He then illustrated the timing of the various phases of the reaction to gluten that occurs in celiac patients. First the epithelial interaction which happens within hours, followed by the innate immunity response (both phases not genetically restricted), and then finally the adaptive response which occurs over a longer timeframe. He also commented on the importance of the timing and the amount of gluten introduction into the diet of infants predisposed to celiac disease, reminding us that it's now a given that introducing gluten during the first 3 months of life facilitates the development of celiac disease, while we still don't know exactly what would be the best time window. There are very limited data from Colorado that delaying gluten introduction past 7 months may be risky, but there seems to be now some preliminary evidence (from ongoing studies in Italy and from a multicenter study he is leading in the US) that actually gluten introduction after the age of 12 months might be beneficial. I think, however, that the most important part he focused on is the importance of microbiome. This is truly a quickly expanding field: in the past few years we have seen a number of papers [1–7] showing that the microbiome in celiac children is different from that of the normal population. This is not the result of the inflammation because this holds true even after a long time on gluten-free diet. So, there is a hint there that the interplay between the microbiome and the mucosal immunity might be exploited in order to prevent celiac disease.

Nicolas Stettler told us about the importance of diet and later development of obesity. This is of course a very hot issue in all the western countries where the obesity epidemics seems to be out of control. There was an interesting discussion on the methods of measuring body fat: BMI seems to be the most easily available, but it has its limitations; the DXA scan has even more limitations as *William Klish* also pointed out; MRI could be useful, and measuring

the skin fold, although easily accessible and time honored, is prone to a number of errors. An important issue was commented by *Nicolas Stettler*: the association between duration of breastfeeding and later development of obesity. The preventive effect of breastfeeding, something we all gave for granted, was instead challenged by a prospective intervention study done in Belarus where actually such a correlation was not clearly found. The importance of early feeding (in some cases even feeding in the very first week of life!) on the subsequent development of obesity was well illustrated by a number of studies, opening up meaningful scenarios for a preventative intervention.

Graeme Jones brought us to Tasmania and its beautiful landscapes. His studies on a stunning 20% of Tasmanian children seem to be quite representative of the whole population; we thus learned how maternal diet during pregnancy affects the long-term bone mineral density in the offspring at the age of 8 and even at the age of 16. It is also interesting that maternal diet high in fat bore a negative and lasting effect on bone mineral density.

And finally, last but certainly not least, we were brought back to mice and dogs with *Martin Holzenberger* who told us about longevity and introduced the concept of our 'disposable soma'. Dietary restrictions in animals extend longevity, and the data were fascinating: IGF-I receptor, growth hormone and insulin appear to have a complex interplay that not only influences our metabolism and our nutrition, but also our life expectancy.

In the end, I would like to try to have a kind of 'super synthesis' of what was said so far, and especially today, so to come up with some messages which may be worth thinking about. Perhaps the most crucial message is that maternal diet is important. Far-reaching nutritional consequences of maternal diet during pregnancy may not have been so obvious before these presentations: think of what we have learned about the negative and prolonged impact of excess fat in mother's diet. The implications not only impinge on the child's future dietetic choices, but also on his/her future bone health. After birth, the preferred nutrition once again is by breastfeeding; but if this is not possible, perhaps one should give serious considerations to lower caloric feeds during the first week of life, especially in light of our 'obesogenic' environment. What mother eats continues to be important after the baby is born, if she is breastfeeding. In fact, nursing mothers should be encouraged to eat fruits and vegetables, as we have learned that this may well predispose the child toward liking such foods, something really important if one looks at the dismal data on consumption of fruits and vegetables in our young children. The infant's growth must be carefully monitored, as an excessively fast growth may imply not only higher risk of later obesity but also possible shorter lifespan. Many more important conclusions could be drawn from such splendid workshop, and surely we all enjoyed the sharp presentations and the lively discussions throughout these exciting 3 days. Much has been learned, much more needs to be unraveled. Let's all go to work for the future of our children!

Stefano Guandalini

References

1. Tjellstrom B, Stenhammar L, Högberg L, et al: Screening-detected and symptomatic untreated celiac children show similar gut microflora-associated characteristics. Scand J Gastroenterol 2010;45:1059–1062.
2. Tjellstrom B, Stenhammar L, Högberg L: Gut microflora associated characteristics in children with celiac disease. Am J Gastroenterol 2005;100:2784–2788.
3. Di Cagno R, Barbato M, Di Camillo C, et al: Gluten-free sourdough wheat baked goods appear safe for young celiac patients: a pilot study. J Pediatr Gastroenterol Nutr 2010;51:777–783.
4. Schippa S, Iebba V, Barbato M, et al: A distinctive 'microbial signature' in celiac pediatric patients. BMC Microbiol 2010;10:175.
5. Collado MC, Donat E, Ribes-Koninckx C, et al: Imbalances in faecal and duodenal *Bifidobacterium* species composition in active and non-active coeliac disease. BMC Microbiol 2008;8:232.
6. Collado MC, Donat E, Ribes-Koninckx C, et al: Specific duodenal and faecal bacterial groups associated with paediatric coeliac disease. J Clin Pathol 2009;62:264–269.
7. Collado MC, Calabuig M, Sanz Y: Differences between the fecal microbiota of coeliac infants and healthy controls. Curr Issues Intest Microbiol 2007;8:9–14.

Subject Index