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www.metabolic-programming.org/munich2010
Welcome to Munich and to The Power of Programming

On behalf of the Early Nutrition Programming Project (EARNEST), the Early Nutrition Academy (ENA), and the Developmental Origins of Health and Disease Society (DOHaD), and the organizing committee, we are delighted to welcome you to this international conference on ‘The Power of Programming - Developmental Origins of Health and Disease’ at Munich, Germany.

In recent years, strong evidence has accumulated to show that nutrition and lifestyle during pregnancy and infancy exert important long-term effects on development, health and performance. Epidemiological observations are increasingly supported by experimental studies exploring biological mechanisms, as well as by prospective intervention trials providing undisputable evidence for causality in humans. The scientific understanding of such programming effects of early nutrition are of major importance with regards to biomedical research, public health and well-being of people, the practice of nutrition and health care, the economy and wealth of societies, and policy decisions. Obviously, there is ample opportunity for applying this knowledge for preventive approaches. It is therefore both timely and pertinent to review the state of the art, new results and future perspectives in the area of programming research and its applications at this International Conference, which is kindly supported by the General Directorate Research of the European Commission as part of the European Early Nutrition Programming Project (www.metabolic-programming.org), as well as a number of further sponsors. In a multidisciplinary approach, specialists in basic science, epidemiology, clinical medicine and many other fields of research, as well as representatives of advisory and regulatory bodies and food manufacturers are coming together to explore synergistic approaches for further advances in this field. Renowned leaders in their fields will provide state of the art overviews, ably supported by a large number of new investigators presenting their latest findings.

Munich, with its Bavarian charm, the splendid panorama of the Alps, and the many attractions of the city and its surroundings will provide an excellent platform for delegates to share experiences, critically discuss latest findings and develop collaborative approaches for improvement of early nutrition.

We hope you enjoy the Conference and benefit from it, and we wish you a very pleasant stay in Munich!
Welcome from Dr. Antonio Di Giulio

European Commission

The present global financial crisis has significant impacts both on economic sectors and on individuals: in the EU, GDP fell by 4% in 2009, the industrial production dropped back to the levels of the 1990s, and 10% of the population is now unemployed. In the meantime, the world is moving fast and our society is facing challenges such as health inequalities (increase of diet-related diseases, social determinants), demographic changes due to ageing and an increasing world population, pressure on resources and climate change. The EU must now take charge of its future. The new Europe 2020 Strategy puts forward priorities to promote a smart, sustainable and inclusive growth.

Strengthening knowledge and innovation is one the drivers of our future growth. Among others, this requires strengthening our research performance, promoting innovation and knowledge transfer throughout the Union, and ensuring that innovative ideas can be turned into new products and services that create growth and quality jobs and that help address European and global societal challenges.

A major effort is also needed to combat poverty and social exclusion and to reduce health inequalities in order to ensure that everybody can benefit from growth. Equally important will be our ability to meet the challenge of promoting a healthy and active ageing population to allow for social cohesion and higher, longer productivity.

EARNEST is an example of a project responding to the challenge of our society. The obtained results helped in advancing the knowledge on the mechanisms underlying the development/prevention of diet-related diseases (obesity, diabetes, CVD, allergy), enabling healthy ageing, providing recommendations to pregnant women and infants.

The European Commission is proud to contribute to this global effort to improve human health and the quality of life of European citizens and hopes that the opportunities offered in the Framework Programmes will allow policy makers to take evidence-based preventive measures and establish new strategies. Instead of being reactive after the problems have occurred, we should now focus and invest more into prevention. Healthy eating habits and lifestyle are key elements.

I am confident that this international conference on developmental origins of health and diseases will play its role to the fullest in providing a platform for a critical review of current knowledge in this area and in exploring and identifying future opportunities for nutrition research and for innovation of food products.

Dr. Antonio Di Giulio

Head of Unit – Food, Health and Well-being
Directorate-General for Research
European Commission
Welcome from Dr. Wolfgang Heubisch

Bavarian State Minister of Sciences, Research and the Arts

Dear ladies and gentlemen,

It is a great pleasure for me to welcome you to the scientific conference on “The Power of Programming – Developmental Origins of Health and Disease” in Munich, the capital of our Free State of Bavaria. The interdisciplinary research of nutrition during pregnancy and infancy contributes fundamentally to children’s healthy development. At this conference, nationally and internationally renowned scientists also present their findings regarding the long-term effects of maternal and infant diet on a person’s development and metabolism in adulthood. The state-of-the-art environment of the Dr. von Hauner Children’s Hospital at the University Hospital Munich – Ludwig-Maximilians-Universität facilitates substantial and outstanding research in this field.

This university hospital – along with others – bears testimony to Bavaria’s excellent conditions for research in medicine and health care and the fact that the Free State attaches greatest importance to fostering research and science, especially in life sciences. The success of the Munich-based biotechnology cluster “m4 – a new dimension in pharmaceuticals development” is another great example. This cluster won in the second round of the Excellence Cluster Competition launched by the Federal Ministry of Education and Research and will receive considerable funding.

More facts speak for Bavaria as a top research location, for example Bavaria’s accomplishment in the Initiative for Excellence, a joint programme of the federal and state governments. 19% of the total sum of € 1.9 billion of funds go to our Free State, which contributed about € 90 million to the programme.

Furthermore, the Ludwig-Maximilians-Universität Munich, the Technische Universität Munich and the Helmholtz-Centre Munich co-operate in the Munich partner institute of the German Centre for Neurodegenerative Disorders (Deutsches Zentrum für Neurodegenerative Erkrankungen – DZNE) in Bonn, which was founded in the context of the initiative of the Federal Ministry of Education and Research supporting national health research centres. This programme also guarantees the Munich partner institute’s permanent funding.

I would also like to mention the networks BayGene and BayImmuNet, which interconnect institutions in the fields of functional genome research and translational immune therapy across Bavaria. The Bavarian State Ministry of Sciences, Research and the Arts funds both of these highly successful networks.

These are all prime examples of Bavaria as a superb location for research.

So I am more than delighted that this pioneering conference, an integral part of the “European Early Nutrition Programming Project”, takes place here in our Free State. The conference is a chance to present the results of five years of European collaborative research and to deepen the synergistic approaches for further advances in this field.

I wish you inspiring discussions and fruitful encounters at the conference and hope you enjoy your stay here in Bavaria.

Munich, in April 2010

Dr. Wolfgang Heubisch

Bavarian State Minister of Sciences, Research and the Arts
Welcome from Prof. Reinhard Putz

Vice-President of Ludwig-Maximilians-Universität Munich

The Ludwig-Maximilians-Universität is pleased to host this Congress on "Developmental Origins of Health and Disease" and is proud to welcome such a distinguished gathering of scientists from all over the world. On behalf of the university administration, I would like to express my gratitude to all our Munich colleagues, and to thank Prof. Koletzko especially, for taking on the enormous task of organizing such a large and complex meeting. Their willingness to shoulder this extra burden is particularly noteworthy at a time when our clinical institutions are operating under considerable economic pressure, and it underlines their determination to maintain a position at the forefront of the field in the future.

LMU Munich – founded in 1472 – is one of the oldest and largest universities in Germany, and provides instruction and conducts research in both technical and all of the important academic specialties. As well as catering for the needs of a very large body of students, the university has earned a worldwide reputation for the quality of its research activities. A questing academic spirit, dedication to the pursuit of excellence and a commitment to scientific collaboration – qualities that are shared by our students and academic staff alike – form the basis for this achievement. Collaborations that transcend the boundaries of traditional disciplines are the secret of success in modern research. And I am happy to say that the Medical School is one of the leading lights among LMU’s internationally recognized research facilities.

Each of you knows how important direct personal contacts are for mutually beneficial exchanges on questions of scientific and clinical relevance. Such interactions require appropriate conditions, and can only succeed in a stimulating environment. Even a cursory glance at the program makes it clear that this Congress admirably fulfills these conditions.

As Vice-President of the university, and as a medical researcher and colleague, I hope very much that the participants of this congress will catch something of LMU’s academic spirit during their stay in Munich, and that their scientific deliberations here will both benefit their own work and help to advance the field as a whole.

Prof. Dr. Dr. h.c. Reinhard Putz

Vice-President of Ludwig-Maximilians-Universität Munich
Chairman Emeritus of Lehrstuhl I, Dept. of Anatomy
Faculty of Medicine
Welcome from Dr. Angelika Niebler

Member of the European Parliament

Dear Participants,

How many mothers know that what they eat during pregnancy and what they feed their babies might strongly affect their children’s health and potentials as grown-ups? Too few, one must answer taking into account the fact that such health problems as diabetes, vascular and bone diseases, or even autism can be caused by bad nutrition. It is therefore one of the central questions of scientific research on nutrition and food to improve foetal and infant nutrition as well as to analyse and warn about food-related health risks for babies and children. The International Conference on Developmental Origins of Health and Disease in Munich promises to provide an excellent platform for a most valuable discussion on this topic. Based on the evidence that nutrition in early life has major effects on long-term health and well-being, the EU-funded Early Nutrition Programming Project (EARNEST) follows the aim of finding ways to reduce the emergence of major adult diseases caused by bad nutrition and to improve infantile development. EARNEST is a successful example for the interconnection of health research with the development of innovative food products for tackling new challenges in public health.

I am convinced that the “Power of Programming” conference will provide a high-level platform for vivid discussions on future needs of research in this field.

Best regards,

Dr. Angelika Niebler

Member of the European Parliament (MEP)
Dear ladies and gentlemen,

As Chief Technical Officer in the Office of Health and Environment at the City Hall of Munich, it is a honour and great pleasure for me to welcome you to Munich for this Conference.

Over the next few days, prominent scientists from Germany and abroad will present new findings on the effects of early nutrition on health in later life. The insights gained from studies on factors contributing to the development of diseases such as adiposity, diabetes and allergies will no doubt suggest novel approaches of preventing these diseases. They will therefore have a great impact on future policy in the field of public health.

Policy measures aimed at improving the overall state of health of young children in particular have enjoyed high priority in our city for the last several decades.

Every year, on World Breastfeeding Day, the Marienplatz in the city centre hosts events highlighting the advantages of breastfeeding. The Health and Environment Office has also organized and implemented a campaign to encourage breastfeeding in accordance with the directives of the European Union's action plan. Advisors are being trained and information sessions on breastfeeding are being offered throughout the city to make mothers more aware of the health benefits of the breastfeeding practice.

In my view, one of the most significant initiatives taken by Munich’s Health and Environment Office has been the introduction of a Visiting Service staffed by qualified paediatric nurses. This service which I would regard as a model, not only for Germany but for Europe as a whole, is designed to enhance child health and now reaches 27% of all children in the city under the age of 12 months. The nurses provide advice and support to young families on health matters, helping to avert sudden infant death, reduce the incidence of allergy and obesity in young children, and prevent accidents in the home. Their work contributes to improving the quality of the mother-child relationship and facilitating child development at all levels. In 2009, we also introduced the Munich Model of Early Assistance, a focused and mandatory programme of social services directed specifically toward the most vulnerable families. The provision of counselling and guidance on nutritional issues is a significant aspect of these programmes. The results of your research will therefore be of great practical significance for the work of our staff of children’s nurses.

Public health policy in Munich is particularly concerned to better the lot of children from socially deprived family backgrounds because they are especially prone to the negative effects of a lack of exercise and are at greater risk of becoming overweight, as shown by the KiGGS Study recently carried out by the Robert Koch Institute. Clarification of the relationships between early nutrition, metabolic programming and the subsequent emergence of harmful conditions like cardiovascular disease, obesity, diabetes and allergies, will inevitably lead to new preventive strategies. Disadvantaged children stand to benefit most from such advances. In this respect, your work has the potential to advance the task of achieving equality of opportunity for all our children.

We in the Public Health Service here in Munich are looking forward to learning about your results. I am sure you will all profit from stimulating scientific discussions at this meeting. I wish you every success and hope you will enjoy your stay in our city.

Joachim Lorenz
Referent für Gesundheit und Umwelt
Landeshauptstadt München
Meeting Organizer

The Early Nutrition Programming Project (EARNEST), the Early Nutrition Academy (ENA) and
the Developmental Origins of Health and Disease Society (DOHaD)

in collaboration with the:
European Academy of Nutritional Sciences
European Society for Paediatric Gastroenterology, Hepatology and Nutrition
German Society of Nutrition
International Society for the Study of Fatty Acids and Lipids
International Union of Nutritional Sciences

Meeting President

Berthold Koletzko

EARNEST Co-ordinator and ENA Managing Director
Ludwig-Maximilians-University of Munich, Germany

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Ricardo Uauy (IUNS) University of Chile
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Scientific Information

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www.metabolic-programming.org
Diamond Sponsors

Abbott Nutrition Health Institute / Abbott Nutrition, Columbus, USA

Danone Baby Nutrition / Danone Research, Schiphol / Wageningen, Netherlands

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Biovitrum AB, Hackås, Sweden

Martek Corp., Columbia, USA

DSM Nutritional Products Ltd., Basel, Switzerland

Laboratorios Ordesa S.L., Sant Boi de Llobregat, Spain

Fresenius Kabi Deutschland GmbH, Bad Homburg, Germany
The Power of Programming – Developmental Origins of Health and Disease

Scientific Programme

Programme subject to change

Thursday, 6th May 2010

10.00 – 11.00
Lecture Hall III + IV

Opening Session: Welcome and Introduction

European Commission supported Research – Antonio Di Giulio - Head of Unit Food, Health and Well-being, DG Research, European Commission

Lifescience Research in Bavaria – Friedrich Wilhelm Rothenpieler, Head of Department at the Bavarian State Ministry of Sciences, Research and the Arts

Lifescience Research at the University of Munich - Reinhard Putz, Vice President, Ludwig-Maximilians-University of Munich

Five Years of Collaborative European Research on Early Nutrition Programming - Berthold Koletzko, EARNEST Coordinator and Local Organizer, Ludwig-Maximilians-University of Munich

11.00 – 11.30

Coffee and Tea Break

11.30 – 12.15
Lecture Hall III + IV

Plenary session I: Chairs: Sjurdur F. Olsen, Raanan Shamir
Developmental origins of long-term health – public health implications – Mark Hanson

A.1 Parallel Session – Impact of infant feeding on growth and obesity risk
Berthold Koletzko, Veronica Luque
- Breastfeeding and body composition - Andreas Beyerlein
- Effects of prolonged and exclusive breastfeeding on adiposity, stature and blood pressure in children aged 11.5 years: evidence from the Promotion of Breastfeeding Intervention Trial (PROBIT) - Richard Martin
- Solid introduction and growth in the first two years of life - Veit Grote
- Does early introduction of solids, and especially protein-rich solids, affect growth in infancy and early childhood? - Lenie van Rossem
- Infant protein intake and metabolic and endocrine response - Piotr Socha

B.1 Parallel session – Fetal placental nutrition
Harry McArule, Hans Demmelmaier
- Placental transport in normal and pathologic pregnancies - Gernot Desoye
- Gene expression in the term placenta: effect of maternal BMI and glucose tolerance on uncoupling protein 2 (UCP-2), toll-like receptor 4 (TLR-4) and DNA methyltransferase-1 (DNMT-1) - Jole Martino
- Placental transfer of fatty acids and fetal implications - Elvira Larque
- Iron-deficiency in the pregnant rat results in increased levels of phosphorylated AKT in placenta at D21.5 of gestation - Christine Lang
- Fetal signalling of iron needs - Harry McArule

C.1 Parallel session – Tracking of risk factors from early life to adulthood
Rüdiger von Kries, Andy Ness
- Statistical methods to assess tracking - Ulrich Mansmann
- Growth pattern in childhood and hypertension in adult life in a high birth weight population - Thorhallur Halldorsson
- Will the observed health impact from exposure in early life be sustained? Meta-analyses on tracking of blood pressure and BMI - Michael Toschke
- Is parental obesity important in the tracking of adiposity in mid-childhood? - Pauline Emmett
- Associations of growth trajectories in infancy and childhood with cardiovascular and cognitive outcomes - Kate Tilling

14.00 – 15.00

Lunch Buffet + Poster Viewing
<table>
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<tr>
<th>Time</th>
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| 14.05 - 14.50 | DOHaD Society Annual Business Meeting (AGM)  
Lecture Hall II |
| 15.00 – 15.45 | EANS Executive Board Meeting  
Lecture Hall IV |
| 15.00 – 15.45 | Lecture Hall III + IV  
Plenary Session II: Chairs: Mike Symonds, Rebecca Simmons  
Developmental epigenetic programming: chasing shadows – Claudine Junien |
| 15.45 – 16.15 | Coffee and Tea Break |
| 16.45 – 17.55 | A.2 Parallel session – Weight gain and body composition  
Ricardo Closa, Peter Rzehak  
- Assessment of weight gain: variations according to the reference used - Marie Francoise Rolland Cachera  
- Parental-offspring associations in body mass index in the Norwegian Mother and Child Cohort Study - Caroline Peten  
- Childhood growth and adult body composition and later health - Johan Eriksson  
- Fish oil-supplementation has little effect on growth and body composition in late infancy - Anders Daniel Andersen  
- Short- and long-term effects of feeding hydrolyzed protein infant formulas on growth at 10 years of age: results from the German Infant Nutritional Intervention Study - Peter Rzehak |
|             | B.2 Parallel Session – Epigenetics  
Jaap Joles, Sylvain Sebert  
- The perinatal programming of metabolic diseases - is epigenetic resetting the missing link? - Sylvain Sebert  
- Neonatal overfeeding in mice predisposes to glucose intolerance to offspring (F1) and grand-offspring (F2) of over nourished individuals (F0) through the paternal lineage: Potential role of epigenetics - Thais Pentinat  
- Genomic Imprinting and Epigenetic Programming of Metabolic Disease - Miguel Constancia  
- Evidence that early growth influences adiposity at age 9-13 years and is mediated by epigenetic regulation of gene expression - Alix Groom  
- Epigenetic Regulation of Beta-cell Function - Rebecca Simmons |
|             | C.2 Parallel session – Maternal nutrition: impact on pregnancy outcomes  
Sjurdur F. Olsen, Maria Hermoso  
- Impact of dietary factors in pregnancy on risk of pregnancy complications: results from the Norwegian MoBa cohort - Helle Margrete Meltzer  
- Discordant secular trends in maternal body size and offspring birth weight of term births in France between 1972 and 2003 - Ibrahima Diouf  
- Impact of dietary factors on risk gestational diabetes: Review focusing on epidemiologic evidence - Cuilin Zhang  
- High rate of overweight, obesity, dyslipidemia and hypertension in infants and children from mothers with gestational diabetes mellitus (GDM) - Rainer Stiff  
- The role of oxidative stress and antioxidant supplementation in pregnancy disorders - Lucilla Poston |
| 19.00 | Welcome Reception |
**Friday, 7th May 2010**

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<th>Time</th>
<th>Event</th>
<th>Location</th>
<th>Speakers</th>
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| 08.20 – 09.25 | Industry Forum “The ways for innovation: how to foster collaboration between industry and academia” | Lecture Hall III - Montserrat Rivero (Ordesa), Kristina Timdahl (Biovitrum) | Montserrat Rivero (Ordesa), Kristina Timdahl (Biovitrum)  
|         | • EC research to promote growth of food industry                     |                        | Antonio Di Giulio (DG Research, European Commission)  
|         | • From the idea to the product                                        |                        | Ferdinand Haschke (Nestlé Nutrition Institute)  
|         | • Challenges for industry and academia as consequence from the Health Claims Regulation: The industry perspective |                        | Gunhild Kozianowski (Beneo-Group) |
| 09.30 – 10.15 | Workshop (WS1): How to write a successful research proposal         | Lecture Hall II -     | Margaret Ashwell, Elena Martin-Baudista  
|         |                                                                    |                        |  
|         |                                                                    |                        | • Validation of measures of physical activity in pregnancy exapmplied by findings from the Norwegian Mother and Child Cohort Study - Anne Lise Brantsæter  
|         |                                                                    |                        | • Self-reported physical activity during pregnancy in relation to BMI and blood pressure in adult offspring: Prospective study over two decades - Inge Danielsen  
|         |                                                                    |                        | • Effects of maternal swimming during pregnancy on onset of body weight programming in the overfed offspring - Fang Gao  
|         |                                                                    |                        | • Maternal physical exercise and risk of Gestational Diabetes Mellitus, Gestational Hypertension and adverse birth outcomes: The Mother-Child cohort in Crete (RHEA study) - Manolis Kogevinas |
| 10.15 – 10.45 | Plenary Session III: Chairs: John Mathers, Katherine Mace          | Lecture Hall III + IV  | Susan Ozanne  
|         | Mechanisms of early life programming – current knowledge and future directions |
| 10.45 – 12.20 | A.3 Parallel Session – Early origins of disease: research opportunities through new methods and integration | Lecture Hall III       | Lucilla Poston, Michelle Mendez  
|         | • Drawing causal inferences in epidemiological studies of early life influences - Andy Ness |                        |  
|         | • Relation of Insulin-like Growth Factor-1 (IGF-1) to protein-induced kidney growth in healthy infants: results from a randomized clinical trial - Veronica Luque |                        |  
|         | • Metabolomics and systemic views on early programming               |                        |  
|         | B.3 Parallel session – Programming of bone health                   | Lecture Hall II        | Mary Fewtrell, Katharina Werkstetter  
|         | • Insights into the programming of bone development from the ALSPAC cohort - Jon Tobias |                        |  
|         | • Bone quantitative ultrasound measurements in breast fed and formula fed infants - Francesco Savino |                        |  
|         | • Are early growth and nutrition related to bone health in adolescence? - Christian Malgaard |                        |  
|         | • Insufficient dietary vitamin D intake amongst pregnant women       |                        |  
|         | C.3 Parallel session – Programming of neurodevelopment               | Lecture Hall IV        | Christina Campoy, Tamas Decsi  
|         | • The role of meta-analysis in the evaluation of the effects of nutrition on mental and motor development in children - Hania Szajewska |                        |  
|         | • Folate intake in pregnancy and psychomotor development at 18 months - Charlotta Granström |                        |  
|         | • Prenatal and early postnatal fatty acid status and neurodevelompental outcome at school age |                        |  
|         | Coffee and Tea Break                                                 |                        |  
|         | C.3 Parallel session – Programming of neurodevelopment               | Lecture Hall IV        | Christina Campoy, Tamas Decsi  
|         | • The role of meta-analysis in the evaluation of the effects of nutrition on mental and motor development in children - Hania Szajewska |                        |  
|         | • Folate intake in pregnancy and psychomotor development at 18 months - Charlotta Granström |                        |  
|         | • Prenatal and early postnatal fatty acid status and neurodevelompental outcome at school age |                        |  
|         | Coffee and Tea Break                                                 |                        |  

The scientific programme was organized into sessions and workshops covering a range of topics related to innovation, research proposals, physical activity in pregnancy, and early life programming. Each session included presentations by experts in their fields, along with interactive workshops and discussions to foster collaboration between industry and academia.
**SCIENTIFIC PROGRAMME**

**Friday, 7th May 2010 (continued)**

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<td>12.20 – 13.25</td>
<td>Lunch Break + Poster Viewing</td>
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<td>13.25 – 14.25</td>
<td>Guided Poster Tour</td>
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**A.4 Parallel Session – Perinatal life and diabetes risk**
- Susanne Ozanne, Éva Szabó
  - Early nutrition and risk of type 1 diabetes - experiences from the TRIGR study risk - Mikael Knip
  - The influence of maternal nutrient restriction in late pregnancy and accelerated postnatal growth on plasma insulin and leptin and hypothalamic gene expression following obesity in the sheep - Neele Dellschaft
  - Randomised clinical trials on infant diet and diabetes risk - experiences from the BABYDIET study - Anette Ziegler
  - Long term appetite regulation and metabolic effects observed in low birth weight rats reared artificially on a high protein milk formula - Patricia Parnet
  - Maternal malnutrition programmes a diabetic phenotype

**B.4 Parallel session – Dietary practice in mother and infants**
- Sylvia Scaglioni, Darek Gruszfeld
  - Dietary patterns during pregnancy across Europe - Michelle Mendez
  - Formula feeding is associated with weight gain in early infancy - Seema Mihrshahi
  - Influence of parental attitudes in the development of children dietary practice - Sylvia Scaglioni
  - Dietary patterns during pregnancy and the risk of postpartum depression - Leda Chatzi
  - Introduction of complementary feeding in 5 European countries - recommendations vs. implementation - Sonia Schiess

**C.4 Parallel session – Environmental toxicants and programming**
- Juliette Legler, Martijn Dollé
  - The OBELEX project: prenatal exposure to endocrine disruptors and obesity - Juliette Legler
  - Cohort Study on Infant Atopic Dermatitis and Fetal Exposure to Persistent Organic Pollutants (POPs), Heavy Metals and Brominated Flame Retardants (BFRs) - Chisato Mori
  - Research on environmental toxicants in the Norwegian HUMIS cohort - Merete Eggshoe
  - Non-teratogenic environmental toxicant exposure of organogenesis stage embryos results in osteoporotic bones in adults - Arkady Torchinsky
  - Developmental exposure to endocrine disruptors and the obesity epidemic - Retha Newbold

- Lecture Hall II -
  • Early Nutrition, Fat Quality and Health in Later Life - Atul Singhal
    - Key concepts in nutritional programming - Atul Singhal
    - Does the n-6/n-3 fatty acid ratio in the diet of pregnant women influence early adipose tissue development – the INFAT study? - Hans Hauner
    - Impact of dietary fat quality in early life on body composition - Eline van der Beek
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<td>16.05 – 16.30</td>
<td><strong>Coffee and Tea Break</strong></td>
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<td>16.30 – 18.05</td>
<td><strong>A.5 Parallel session – Early fish exposure and later health outcomes</strong></td>
<td>Hall III</td>
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<td>Philip Calder, Sjurdur F. Olsen</td>
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<td>- The Salmon in Pregnancy Study (SIPS): Study design and effects on maternal and infant nutritional status - Liz Miles</td>
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<td>- Genes and nutrition: The impact of fatty acid desaturase (FADS) polymorphisms on long-chain polyunsaturated fatty acid levels - Eva Lattka</td>
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International Society for Developmental 5
Origins of Health & Disease (DOHaD Society)
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Differences in nutritional experience during sensitive periods in early life, both before and after birth, can programme a person's future development, metabolism and health. Better scientific understanding of Early Nutrition Programming holds enormous potential for implementing preventive strategies to enhance the long-term health, well-being and performance of people. This could not only reduce costs of health care and social services, but could as well enhance wealth of societies. The Early Nutrition Programming Project brings together a multi-disciplinary team of international scientists and leaders in key areas of the early nutrition programming field from 40 major research centres across 16 European countries. The project with a total budget of 16.5 million Euros is funded by the EC under the Sixth Framework Programme for Research and Technical Development and is co-ordinated by the Children's Hospital at Ludwig-Maximilians-Universität of Munich. The integrated programme of work combines experimental studies in humans, prospective observational studies and mechanistic animal work including physiological studies and cell culture models, with molecular biology techniques. The project started in 2005 and will run to October 2010. After the end of the project, the Early Nutrition Academy (http://www.metabolic-programming.org/academy.htm) will continue to serve as a platform for exchange of information, scientific collaboration and training activities in the area of programming. This presentation will highlight some of the scientific results and achievements and the efforts of the Early Nutrition Programming Project in respect to training and dissemination.

I: Developmental Origins of Long-Term Health – Public Health Implications

M A Hanson
Institute of Developmental Sciences, University of Southampton, UK

Chronic, non-communicable disease poses a major threat to global health and to economies in both developed and developing countries. Risk of such disease is established in part during early life, when environmental influences transduced by the mother, including her diet, body composition and exposure to stress, affect the development of her fetus and newborn, establishing its responses to later environment. If these cues are inaccurate, e.g. unbalanced maternal diet or nutritional transition between generations through migration, the individual's responses are mismatched to environmental challenges, leading to greater risk of disease. Maternal and child undernutrition remain enormous problems throughout the developing world, but in developed societies many people also have a poor lifestyle. Thus adverse consequences of over- and under-nutrition co-exist. New evidence suggests that the resulting risk can be transmitted down multiple generations. The consequences extend to reproductive health, behavioural, cognitive problems and risk of some cancers. Epidemiological, human clinical and basic science research has indicated underlying mechanisms many of which involve epigenetic processes, which can serve as early markers of later risk and which are in principle reversible. An urgent priority is to assess such early markers of risk and to implement the necessary complex interventions.

II. Developmental epigenetic programming: chasing shadows

Claudine Junien, Linda Attig, and Anne Gabory
BDR Biologie du Développement et Reproduction Developmental Biology and Reproduction UMR INRA-ENVA-CNRS 1198, Domaine de Vilvert, Batiment 230, F-78352 Jouy en Josas. claudine.junien@jouy.inra.fr

The ways in which epigenetic modifications fix the effects of early environmental events, ensuring sustained responses to transient stimuli, which result into modified gene expression patterns and phenotypes later in life, is a topic of considerable interest. Increasing numbers of genome-wide studies based on high-throughput technologies and focusing on humans and mice have revealed additional complexity in epigenetic processes, highlighting the importance of stage-, sex-, and cell-specific epigenetic landscapes, and of crosstalk between the different epigenetic marks. This paper focuses on recently discovered mechanisms and calls into question prevailing views about the dynamics, positions and functions of relevant epigenetic marks. Animal models, including mice, rats, sheep, pigs and rabbits, remain a vital tool for studying the influence of early nutritional events on adult health and disease. In recent months, a number of studies focusing on the Developmental Origin of Health and Disease (DOHaD) and metabolic programming have identified links between early nutrition, epigenetic processes, and long-term illness. They have demonstrated the existence of an on-going self-propagating epigenetic cycle, of metabolic memories and ageing processes. However most epigenetic studies have only addressed the long-term effects on a small number of epigenetic marks, at the global or individual gene level, of environmental stressors in humans and animal models. Despite recent progress, we are still far from understanding how, when and where environmental stressors disturb key epigenetic mechanisms. Thus identifying the original key marks and their changes throughout development, during an individual's lifetime or over several generations, remains a challenging issue.

Key-Words: Epigenetics – Histone modifications - DNA Methylation - Nutrition – DOHaD– Environment - Fetal Programming
III. Mechanisms of early life programming – current knowledge and future directions

Dr Susan Ozanne,
Institute of Metabolic Science, University of Cambridge, UK

It is over twenty years since epidemiological studies that revealed that there was a relationship between patterns of early growth and subsequent risk of diseases such as type 2 diabetes, cardiovascular disease and the metabolic syndrome. Studies of identical twins, individuals who were in utero during periods of famine and animal models have provided strong evidence that the early environment, including early nutrition, plays an important role in mediating these relationships. The concept of early life programming is therefore widely accepted. However the mechanisms by which a phenomena that occurs in early life can have long-term effects on the function of a cell and therefore metabolism of an organism many years later are only starting to emerge. These include: (1) Permanent structural changes in an organ resulting from suboptimal levels of an important factor during a critical period of development. Such an example is the requirement of the neurotrophic action of leptin during a restricted period of development during neonatal life. (2) Persistent alterations in epigenetic modifications (e.g. DNA methylation and histone modifications) leading to changes in gene expression. Several transcription factors are susceptible to programmed changes in gene expression through such mechanisms. (3) Permanent effects on regulation of cellular ageing. Increases in oxidative stress leading to macromolecular damage, including that to DNA and specifically telomeres can contribute to such effects. Further understanding of such processes will enable the development of preventative and intervention strategies to combat the burden of common diseases such as type 2 diabetes and cardiovascular disease.

IV. Global impact of programming

Ricardo Uauy,
Public Health Nutrition London School of Hygiene and Tropical Medicine, University of London, UK

Nutrition throughout the life course has great significance not only for women and children but also for the health and wellbeing of society. The role of pre-and pregnancy nutritional status can no longer be ignored since it impacts not only conception, gestation, growth and development of the fetus and infant but it also has short and long term consequences on health and disease patterns and economic productivity at later stages of life. Nutrition marks structurally and/or functionally the development of the fetus with lifelong impacts. The magnitude, timing and duration of the nutritional insults define the final impacts; patterns of gene expression and epigenetic changes affects transcription factors controlling multiple target genes thus explaining the consequences on human and economic development. Optimization of environmental conditions affecting early growth should lead to effective approaches to optimize fetal growth to achieve not only an adequate birth-weight but also maximize lifelong health preventing adult disease and disability. Malnourished populations are also more vulnerable to infections and poor length growth affecting brain development and cognitive performance. Labor productivity and income will be lower than that observed in well nourished peers. Poverty will only be broken by actions to improve early nutrition and linear growth. Malnutrition in early life is no longer a health or an ethical-social dilemma but the cause of self perpetuating constraints on economic development. Thus, the impact of early programming has major human-socio-economic implications for all countries, especially societies undergoing a rapid nutrition transition.

Closing Session:

Programming Research: where are we and where do we go from here?

Berthold Koletzko¹, Mike Symonds², Sjurdur Olsen³, for the Early Nutrition Programming Project
¹Dr. von Hauner Children’s Hospital, Univ of Munich Medical Centre, München, Germany, ²University of Nottingham, United Kingdom,
³Danish Epidemiology Science Centre, Statens Serum Institut, Copenhagen, Denmark

Convincing evidence has accumulated to show that both pre- and post-natal nutrition pre-programme long-term health, well-being and performance until adulthood and old age. This is supported by three separate lines of evidence, including lifetime experimental studies in animals, historical and prospective observational studies in humans, and experimental, hypothesis-testing trials in humans with long-term follow-up. There is enormous potential in applying this knowledge for preventive approaches with regards to improving the health and well-being of the population, to reducing costs for health care and social services, and for enhancing productivity and wealth of societies. To achieve such benefits, solid science based knowledge is required to assess the effect sizes of early life programming in contemporary European populations with regard to specific outcomes related to long term health and burden of adult disease, to characterize underlying mechanisms, to establish sensitive time periods during which these exposures act, and to understand potential effect differences in different subgroups of the populations characterized e.g. by genetic predisposition or gender. The results of this research should lead to conclusions on best nutritional practice in pregnancy, lactation and infancy. In this presentation, we shall review the state of the knowledge, identify some key issues that need to be resolved, and describe opportunities for future research.
Breastfeeding and body composition
Andreas Beyerdlein,
Institute of Social Paediatrics and Adolescent Medicine, University of Munich, Germany

According to the priming concept, factors such as nutrition in early life may programme a person’s morbidity and health in later life. Amongst other factors, breastfeeding has been hypothesized in recent years as a potential priming factor of overweight. From a mechanistic point of view, a protective effect of breast- vs. formula-feeding with respect to later overweight appears plausible. Several observational studies found evidence for a small protective effect with respect to overweight in childhood. Three meta-analyses reported significant protective effects of breastfeeding against overweight in later life, whereas another one found no effect of breastfeeding on mean body mass index (BMI) after adjustment for confounding factors. These seemingly inconsistent results might potentially be explained by different effects of breastfeeding on normal- vs. overweight children.

Evidence from interventional studies is limited. A randomized trial failed to confirm an effect of breastfeeding promotion on children’s BMI, but may have lacked statistical power, since rates of breastfeeding were relatively similar in the intervention and control group.

In summary, protective priming effects of breastfeeding on later overweight appear possible, but are difficult to prove. While observational studies have to deal with confounding issues, interventional studies on breastfeeding promotion may lack power.

Effects of prolonged and exclusive breastfeeding on adiposity, stature and blood pressure in children aged 11.5 years: evidence from the Promotion of Breastfeeding Intervention Trial (PROBIT)
Richard Martin 1, Rita Patel 1, Michael Kramer 2, Lauren Guthrie 3, Konstantin Vilchuck 2, Natalia Boghdanovich 4, Natalia Sergeichick 5, Matthew Gillman 3, George Davey Smith 1, Emily Oken 3, Irina Mitroshenka 4
1 University of Bristol, BRISTOL, UNITED KINGDOM
2 McGill University, MONTREAL, CANADA
3 Harvard University, UNITED STATES OF AMERICA
4 Centre for Maternal and Child Health, MINSK, REPUBLIC OF BELARUS

Background: Observational studies which suggest that prolonged, exclusive breastfeeding reduces childhood obesity and cardiovascular disease risk may be confounded by factors influencing maternal choice to breastfeed. Methods: Cluster-randomized controlled trial (PROBIT) involving 31 maternity hospitals and 17,046 children in Belarus, randomized to usual care (15 hospitals) or to a breastfeeding promotion intervention based on the WHO/UNICEF Baby Friendly Hospital Initiative (16 hospitals). The intervention substantially increased breastfeeding duration and exclusivity compared to the control arm (43% vs 6% exclusively breastfed at 3 months). At 11.5 years the children were followed up, including measures of adiposity, stature and blood pressure. We conducted an intention-to-treat analysis based on data on from the first 11,674 (68%) followed up, accounting for clustering by hospital.

Results: Cluster-adjusted mean differences in experimental minus control groups were 0.16 kg/m² (95% CI: -0.08, 0.41) for BMI, 0.44% (-0.15, 1.03) for body fat, 0.40 cm (-1.18, 1.99) for waist circumference, 0.07 mm (-1.57, 1.71) for triceps and 0.09 mm (-0.73, 0.91) for subscapular skinfold thicknesses, 0.55 cm (-0.49, 1.59) for standing height, -0.08 cm (-0.61, 0.78) for trunk length, 0.51 cm (-0.15, 1.17) for leg-length, and 1.15 mmHg (-1.06, 3.37) for systolic and 0.88 mmHg (-0.54, 2.30) for diastolic blood pressure. The cluster-adjusted odds ratio for obesity (BMI =95th percentile), comparing experimental versus control groups, was 1.17 (0.92, 1.50).

Controlling for baseline co-variables yielded similar results. Conclusion: These results do not support a long-term beneficial effect of prolonged and exclusive breastfeeding on adiposity, stature or blood pressure in childhood.

Solid introduction and growth in the first two years of life in formula-fed children
V. Grote 1,2, S. Schiess 1, B. Koletzko 2, for the European Childhood Obesity Trial Study Group
1Dr. von Hauner Children’s Hospital; 2Institute of Social Paediatrics and Adolescent Medicine, Ludwig-Maximilian University Munich, Germany

Objectives: We tested the hypothesis that the timing of solid introduction has no influence on growth during the first two years of life.

Methods: Term, formula-fed infants were recruited after birth in five European countries. Standardized anthropometric measurements were taken at recruitment, and at 3, 6, 12, and 24 months. The week of solid introduction was determined by questionnaire and by prospective three day weighed food records at monthly intervals. Linear regression analysis and multilevel growth models were used for analysis.

Results: The median age at solid introduction of 671 children was 19 (25.75. perc. 17-21) weeks. About 7% of the children were introduced to solids before the end of the 3rd months of life. There was a statistically significant difference in growth pattern over the first 24 months of life by weak of solid introduction for weight-for-age (p=0.005) but not for weight-for-length (p=0.084) and length-for-age (p=0.127). Whereas early introducers (< 13 weeks) “catched-up” growth between baseline and 6 months and transiently attained a higher weight-for-length at 6 months than all other children, the late introducers (>22weeks) had less weight and length gain between baseline and 3 months and continued at a lower weight-for-age trajectory than all other children until 24 months of age. Both solid introduction groups in between (14-18 and 19-22 weeks) had similar growth patterns.

Conclusion: Solid introduction is associated with growth patterns during the first 2 years of life. However, there is no linear effect of time of solid introduction on growth.
Does early introduction of solids, and especially protein-rich solids, affect growth in infancy and early childhood?

Liene van Rossem, Jessica Kieffe-de Jong, Vincent Jaddoe, Albert Hofman, Johan Mackenbach, Henriette Moll, Hein Raat

Erasmus MC - University Medical Center Rotterdam, ROTTERDAM, NETHERLANDS

Background: The association between infant feeding and obesity is still unequivocal as well as the mechanisms behind this association. We hypothesized that early solid introduction, and especially protein-rich solids, affect growth indicators.

Methods: Mothers of children (n=3225) in a birth cohort provided information on infant feeding from questionnaires at 2, 6, and 12 months. Height and weight were measured at 11 time points from 1 to 36 months. Standard deviation scores for growth were calculated from national references. We used longitudinal multivariable regression methods to obtain estimates for solid introduction.

Results: Weight-for-age z score was higher in children introduced solids between 3 and 6 months than those introduced solids after 6 months of age (b=0.08, 95% CI: 0.02, 0.14). This estimate was 0.04 (95% CI: -0.02, 0.10) for protein-rich solids. After adjustment for birth weight, gestational age, history of allergy, breastfeeding, mother’s educational level, ethnicity, body mass index, and smoking, weight-for-age z score ceased to be significant for both solids and protein-rich solids (b=0.04, 95% CI: -0.02, 0.10 and b=0.05, 95% CI: -0.01, 0.11). Additional adjustment for history of hospital admission attenuated the results further (b=0.003, 95% CI: -0.09, 0.09 and b=0.0004, 95% CI: -0.09, 0.09 for introduction of solids and protein-rich solids respectively). Height-for-age and weight-for-height showed similar effects.

Conclusion: Early introduction of solids is associated with growth but this is mainly attributable to environmental factors particularly hospital admission in first year of life. These data do not support a role for the influence of early introduction of protein-rich solids on growth.

Infant protein intake and metabolic and endocrine response

P. Socha1, V. Grote2, D. Gruszfeld1, B. Koletzko2 and the CHOP team

1Childrens Memorial Health Institute, Warsaw, Poland; 2Dr. von Hauner Children's Hospital, University of Munich Medical Centre, Munich, Germany

Observational studies point to protein intake in early infancy as an important risk factor for later obesity, but information about potential mechanisms is very limited. The CHOP study examined the influence of protein intake in infancy on serum amino acids, insulin secretion and parameters of the IGF-1 axis. Breast fed infants and two randomized groups of formula fed infants with higher and lower protein intake were compared at the age of 6 months. While a total of 1200 infants from 5 European countries still participated in the study at the age of 6 months, biochemical parameters could be determined in 339 infants on low protein formula, 333 infants on high protein formula and 237 breastfed infants. Essential amino acids and especially the branched chain amino acids were clearly higher in the higher protein group than in the low protein group, which showed similar concentrations as the breast fed group. Total and free IGF were significantly (p<0.0001) increased in infants fed high protein formula [48.40 (27.20-81.80) and 0.60 (0.34-1.11); median (10th and 90th percentile), respectively] when compared to low protein group [34.70 (17.70-57.50) and 0.43 (0.27-0.77)]. IGF-binding protein 2 was increased in the high protein intake group when compared to low protein intake group [765(575-1012) vs. 1090 (865-1438); p=0.001]. C-peptide/creatinine urine concentration ratio was significantly increased in the high protein group [140.55 (80.03-203.80) vs 107.25 (65.16-194.74); p<0.05] indicating increased insulin release with high protein feeding. The results point towards a stimulation of the IGF axis and insulin release by high protein formula feeding that corresponds to higher BMI at age 2 years in the high protein infants. The results document for the first time in a randomized intervention trial the stimulation of IGF by increased protein intake and enable the identification of potential mediating factors for the influence of protein intake on anthropometric development.

B.1: Fetal placental nutrition

Thursday, May 6th 12.20 – 14.00

Human placental transport in normal and pathologic pregnancies

Germot Desoye, Martin Gauster1, Christian Wadsack

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Owing to its position between the maternal and fetal circulation the placenta is key for fetal nutrient supply. Hence, any dysregulation in its transport function may result in fetal growth disturbances such as in diabetes (excess fetal adiposity) or intrauterine growth restriction (IUGR).

Several glucose transporters (GLUT1, GLUT3, GLUT4 and the rare GLUT10-12) were identified and localised. Despite some molecular alterations in diabetes caused by the diabetic environment, maternal-to-fetal transport is unchanged at the placental level and glucose flux appears to be driven by the concentration gradient only. This also holds for IUGR with no changes in GLUTs and maternal-to-fetal transport. Collectively, molecular changes in glucose transporters and transplacental glucose transport are not involved in disorders of fetal growth. At the syncytiotrophoblast microvillous membrane, the placental surface is in contact with maternal blood in the intervillous space, maternal lipoproteins, or components thereof, will be taken up, either by endocytosis (mainly by low-density lipoprotein; LDL) or after hydrolysis of HDL (high-density lipoprotein) by endothelial lipase (EL) and subsequent uptake of fatty acids or cholesterol-esters. In IUGR placentas the LDL composition is altered, which is associated with an upregulation of the LDL receptor. In contrast, the HDL lipid moiety is not modified, and EL as well as the prevailing HDL receptor (SR-BI) are reduced. This suggests that at least the first step in the complex process of maternal-to-fetal transport of lipids is altered in IUGR, and may contribute to the fetal growth impairment in this condition.
Iron-deficiency in the pregnant rat results in increased levels of phosphorylated AKT in placenta at D21.5 of gestation

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Iron-deficient anaemia is a severe health problem during pregnancy, resulting in serious consequences for the mother and her developing fetus. The fetus is smaller, with an increased placenta:fetal weight ratio. It has an increased risk of perinatal death and hypertension as an adult. The mechanisms underlying these outcomes are not clearly understood. The placenta plays the central role in delivery of nutrients from the mother to her fetus, and maternal iron-deficiency may affect cellular pathways in the placenta, hence modifying fetal growth and development. The serine/threonine kinase AKT is involved in regulating cell growth and survival and has been associated with systemic nutrition sensing. In this work we demonstrate that iron-deficiency during pregnancy results in increased levels of phosphorylated AKT in the placenta. This effect is not simply a generic response to iron-deficiency, because the levels of phosphorylated AKT are not altered in maternal liver and there is no correlation between maternal iron-status and levels of phosphorylated AKT. Furthermore, this change in the placenta appears to be tissue specific, since the fetal liver does not show any detectable phosphorylation of AKT and preliminary data indicate that levels in the fetal lung remain unchanged. Thus the changes of phosphorylated AKT levels in the placenta at D21.5 gestation in response to maternal iron-deficiency may contribute to the change in placenta:fetal weight ratio, to altered nutrient delivery and the increased risk of health problems in the offspring. This work was supported by EARNEST and RERAD.
Iron is essential for normal growth and development and the consequences of deficiency in pregnancy can be very serious. Consequently, a series of complex regulatory processes have evolved to protect the fetal supply. The placenta plays the central role in this regulation. In this review, we will examine the mechanisms involved. Iron is carried in the maternal serum on transferrin. Transferrin binds to its receptor on the microvillar membrane of the placenta. The complex is taken up into coated vesicles and the vesicle is acidified. Iron is released and moves into the cytoplasm through a divalent channel, DMT1. Efflux of iron to the fetus is through a protein called ferroportin. At this stage, iron exists as Fe(II) and it is oxidised to Fe(III) by a protein called zyklopen, binds to fetal transferrin and is carried to the fetal liver. A small peptide, called hepcidin, is released from the fetal liver, at a level inversely proportional to iron status. This peptide interacts with the placenta, and regulates transferrin receptor expression. At the same time, an unidentified molecule signals fetal iron requirement to the maternal liver. The system seems to operate effectively until a certain “break-point” is reached, when the maternal liver re-asserts its iron requirement. If the mother cannot keep iron levels above this break point, the fetus will become iron deficient. However, until that point the fetus is protected at the expense of the mother. This very sophisticated system is an excellent example of maternal-fetal communication, mediated by the placenta. This work was supported by Scottish Government, EARNEST and NuGO.

Statistical methods to assess tracking
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In epidemiology, tracking describes the stability of the longitudinal development of an outcome variable. The concept involves early as well as later measurements in life, the maintenance of a relative position within a distribution of values in the observed population over time, and the predictability of later values from early measurements. Therefore, tracking is monitoring of a dynamic evolving process over time but also setting or streaming the manner by which individuals are separated with respect to their personal conditions into groups with different potentials for development. While the first aspect aims at developing a system for the classification of individuals, the second aspect consists in applying it to a population. Both pose different statistical challenges which are called model building and model validation.

The talk introduces basic concepts like tracking coefficients. Longitudinal continuous as well as categorical data will be considered. Then, the talk focuses on model building and model validation in the framework of prediction. It considers the fact that these activities aim to provide tools which should have a good performance on future subject. The implication of this fact on models derived from longitudinal data will be discussed. The talk will consider static as well as dynamic models. A static model uses information from the beginning of a time course to predict events in the future. A dynamic model tries to use the whole past of an ongoing time course to do a similar prediction. It will be described how Bayesian statistics allows handling these ideas.

Growth pattern in childhood and hypertension in adult life in a high birth weight population
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Background: Birth weight and childhood growth have been associated with adult hypertension. The relative importance of each measure and sex specific differences are less well established. Setting: 1333 boys and 1258 girls of high birth weight (mean:3730g), born in Reykjavik, Iceland (year:1912-1932). Changes in childhood body-mass-index (BMI) were calculated over 2-year periods (BMI/year=BMI-growth-velocity) at ages 8-10, 9-11, 10-12, 11-13 years and associations with adult hypertension were explored. Adjustments were made for starting BMI at each 2-year period, birth weight, birth year; and age at outcome measure. Results: Between 8-10 years, no differences in childhood BMI were observed in boys who later became hypertensive compared to normotensive individuals. From 11-13 years of age, boys who became hypertensive had higher BMI compared to normotensive individuals with mean difference at 13 years being 0.4kg/m2 (95%CI: 0.2, 0.7). For boys, BMI-growth-velocity had a significant U-shaped association with adult hypertension. Using as referent the 2nd quintile in the BMI-growth-velocity distribution between 11-13 years, boys in the lowest quintile had adjusted odds ratio of 1.8 (95%CI 1.2, 2.6) for developing hypertension, while the corresponding odds ratio was 2.1 (95%CI 1.4, 3.1) for the highest quintile. Eliminating those overweight in childhood (5%) did not change the association. BMI-growth-velocity was not associated with hypertension in girls and modest non-significant association was observed for birth weight in both sexes. Conclusions: Imboys of high birth weight, slow and accelerated growth of BMI was associated with adult hypertension, independent of birth weight and starting BMI at the growth period.
High blood pressure (HBP) and obesity are associated with later cardio- and cerebrovascular disease. Several studies have reported altered frequencies of HBP or obesity after certain perinatal exposures. The estimate of tracking of BP or body mass index (BMI) varied among different population based studies. Systematic reviews and meta-analyses were performed to estimate the amount of BP tracking or BMI tracking from childhood to adulthood.

A total of 30 studies including 28,046 individuals and 305,378 person years could be identified for studies on blood pressure tracking while the BMI tracking analysis resulted in 48 papers on 55,185 individuals (799,806 person years). Tracking of BP was low to moderate with an overall adjusted systolic BP correlation coefficient of 0.44 between 10 and 11 years and decreasing to 0.37 between 10 and 20 years. Tracking of BMI was strong with values >=0.78 after 1 year. Main variables associated with degree of tracking were length of time-lag between measurements and age at baseline. Due to low to moderate BP tracking from childhood to adulthood regular blood pressure controls are also needed in children with normal blood pressure measurements helping to possibly identifying hypertensive children earlier. Slight short-term beneficial effects on BMI due to perinatal exposures might have a higher sustainability compared with slight effects on BP.

**Associations of growth trajectories in infancy and childhood with cardiovascular and cognitive outcomes**

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Objective: To investigate whether growth in early-life is associated with cardiovascular outcomes at ages 6.5 and 12.5 years and atopy at age 6.5 years.

Design Prospective cohort study nested in a randomised trial.

Participants 10,494 children from Belarus who were born in one of 31 hospitals participating in a cluster randomised trial of breastfeeding promotion, with multiple measures of height and weight from birth to age 6.5 years. We analysed all 13 childhood growth measurements to develop a best-fitting linear spline random-effects model with 2 knots. The spline models were used to generate 4 random effects coefficients for weight and for height for each child. Each coefficient denotes an individual’s deviance from average birth weight, birth length or weight or height velocity at each time period; together, the coefficients are a within-subject summary of each child’s weight and height curves from birth to 5 years. The coefficients were converted into age-standardised z-scores to render them directly comparable.

Main outcome measures Systolic and diastolic blood pressure (mmHg) and BMI (kg/m2) measured at ages 6.5 and 12.5 years. Asthma, eczema and allergy measured at 6.5 years. Sex-specific OLS was used to investigate associations of each coefficient with blood pressure, controlled for hospital and baseline confounders. Results will be presented.

Conclusion: Summarising growth using data-derived velocities can help identify relationships between early growth and later outcomes. Multilevel models have several advantages over usual methods, including no restriction to measures at arbitrary times or individuals with complete data, and allowance for measurement error and colinearity.
Assessment of weight gain: variations according to the reference and growth parameter used

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Many studies have investigated the association between early growth and future obesity, but the methods vary considerably. According to the studies, various references are used and different growth parameters are considered. The CDC, French, UK and Dutch references were compared with the WHO standards. All references showed marked lower values for weight, length and BMI as compared to WHO standards during the first months of life. The difference may be attributable to the selection criteria such as feeding practice. Epidemiological and clinical studies have analysed the variations in the evaluation and interpretation of the child growth according to the reference used.

Rate of growth is generally investigated on the basis of an increase of weight between two dates, but the impact of other anthropometric indicators have received less attention. On the basis of a longitudinal study, we have compared the predictive value of adult BMI using either weight, length or BMI gain. As in previous studies, we found that adult overweight is best predicted by weight gain, but after adjustment for length gain, weight gain had similar predictive value as that of length or BMI gain.

In spite of their similar predictive values, it can be hypothesised that the different growth parameters may be associated with different risks at adult age.

In conclusion, the reference used to assess growth may have an impact on the interpretation of growth process. In addition, in studies investigating the consequences of rapid growth, it seems important to consider and differentiate the different growth parameters.

Parent-offspring associations in body mass index in the Norwegian Mother and Child Cohort Study

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Objective: The potential effect of over nutrition during pregnancy on offspring adiposity is assessed, by comparing the association between maternal prepregnancy BMI and offspring BMI at age three with the paternal-offspring association in BMI. Further, the effect on these associations of several social and environmental determinants of offspring BMI is investigated.

Material and methods: This study included parents and their offspring recruited during pregnancy in 1999-2008 in the Norwegian Mother and Child Cohort Study conducted by The Norwegian Institute of Public Health. Linear regression analyses were based on data from self-administered questionnaires during and after pregnancy.

Preliminary results: 20,117 parent-offspring trios were included. The mean BMI at age three was 16.1 kg/m², mean maternal BMI was 24.2 kg/m² and paternal BMI was 25.8 kg/m². After adjustment for the other parent’s BMI, the results showed an increase in offspring BMI of 0.027 kg/m² (P < 0.001) per unit increase in maternal BMI (1 kg/m²), and of 0.035 kg/m² (P < 0.001) per unit increase in paternal BMI. Similar results were found when adjusting for social and environmental determinants of offspring BMI. Adjusted analyses using z score BMIs showed increases of 0.062 and 0.063 standard deviations (SD) in offspring BMI, respectively, for mother’s and father’s increase in BMI by one SD.

Conclusion: Our results show similar associations between maternal-offspring and paternal-offspring BMI. Thus, the results do not provide support for the effect of over nutrition during pregnancy on offspring BMI at age three in a large general population.

Childhood growth and adult body composition and later health

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Much evidence suggests that the pace and pathways of early growth are major factors associated with the development of type 2 diabetes, body composition and related metabolic disorders. Findings in the Helsinki Birth Cohort Study, comprising 13 345 individuals born 1934 – 1944, of whom 2003 have been studied in clinically, will be reviewed. Small birth size and slow growth during the first 2 years, are associated with coronary heart disease and stroke in adult life. This path of growth is also associated with an atherogenic lipid profile. Low birth weight is linked to lower lean body mass later in life. A 1 kg increase in birth weight corresponded in men to a 4.1 kg and in women to a 2.9 kg increase in adult lean body mass. Low birth weight is also related to higher body fat percentage after adjustment for adult BMI. Rapid gain in BMI before the age of 2 years increased adult lean body mass without excess fat accumulation, whereas rapid gain in BMI in later childhood, resulted in relatively larger increases in fat mass. The risk of type 2 diabetes and IGT was increased by low weight gain between birth and 2 years. We are beginning to understand that adult degenerative diseases are associated with different patterns of early growth. Yet it is not clear what optimal growth is and how it can be achieved.
Dietary marine n-3 long-chain polyunsaturated fatty acids (LCPUFA) have in animals been shown to affect development of adipose tissues. In humans, increased postnatal n-3LCPUFA-intake has generally been shown not to influence infant growth, but none of the studies have aimed at investigating the impact on adipose tissue growth. We performed a double-blind intervention study, where 154 healthy Danish infants were randomly allocated to supplementation with (5ml/d) fish oil (FO) or sunflower oil (SO) from 9 to 18 months of age. The primary endpoints were z-scores of anthropometric assessments of body size and composition. The relative content of fatty acids (FA%) in erythrocytes (RBC) was determined as a biomarker of compliance. The estimated median oil intake of the 133 completing infants was 3.8 (25-75 percentile=3.2-4.2) g/d with no difference between groups. The FO-group infants had a larger increase in RBC n-3PUFA than those in the SO-group (12.20.7 (meanSE) vs. 2.00.4 FA%, p<0.001) and a larger decrease in n-6PUFA (-8.90.7 vs. -0.90.6 FA%, p=0.001). Adjusted ANCOVA-models showed no effects of n-3LCPUFA-supplementation on z-scores for height, weight, BMI or skin-fold (SF)-thicknesses. However, at 18 months infants in the FO-group had a lower SF-index (triceps/sub-scapular) than the SO-group (p=0.02). Furthermore, the consumed amount of oil, irrespective of type, affected both triceps (p=0.02) and sub-scapular (p=0.04) SF-thicknesses. This study shows no effect of n-3LCPUFA intake on adipose tissue mass, but indicates an influence on peripheral vs. central subcutaneous fat deposition. The adipogenic effect of oil intake already in infancy could be of public health concern.

Background: We previously found only short-term effects, but no long-term effects of feeding hydrolyzed formulas on growth in a randomized trial (AJCN 2009; 89:1846-56). The 10 years follow-up of the GINI-birth cohort-study allows an analysis beyond age 6 years.

Objective: To investigate potential differences in body-mass-index (BMI) over the first 10 years of life between infants fed by partial-ly-hydrolyzed-whey (pHF-W), extensively-hydrolyzed-whey (eHF-W), extensively-hydrolyzed-casein (eHF-C), cow's-milk-formula (CMF) and infants exclusively breastfed (BF) for the first 16 weeks of life.

Design: Prospective randomized double-blind trial of full-term neonates with atopic heredity in the German birth cohort GINI followed through the first 10 years of life. Intention-to-treat (ITT) and per-protocol (PP) analyses of absolute and WHO-standardized-BMI-trajectories for 1840 (pHF-W: n=253; eHF-W: n=265; eHF-C: n=250, CMF: n=276; BF: n=796) infants.

Results: No significant differences in absolute or WHO-standardized-BMI-trajectories were found between the pHF-W, eHF-W, eHF-C, CMF and BF-groups after the first year of life up to age 10 years; except a non-significant tendency for higher BMI-values for infants fed extensively hydrolyzed formulas (eHF_W, eHF-C) between 6 and 10 years. However, in contrast to the other formula groups the eHF-C group both ITT and PP analyses showed a significantly slower sex-adjusted BMI-gain through the 8th to 48th week of life (-0.1 to -0.2 lower BMI-z-score). Analyses of weight and length revealed that this difference is due to slightly diminished weight-gain in the first year of life and not differences in length gain.

Conclusions: Extension of the follow-up period from 6 to 10 years for this randomized trial confirmed that no longterm consequences on BMI are to be expected irrespective of the hydrolyzed formula fed. However, feeding extensively-hydrolyzed-casein formula results in a transient lower weight-gain in the first year of life.

The perinatal programming of metabolic diseases – is epigenetic resetting the missing link?

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Adult health is critically dependent on early life growth performance and maternal nutrition1 which may independently impact upon insulin sensitivity, body composition and overall energy homeostasis. Since the publication of Hales and Barker’s ‘thrifty phenotype hypothesis’, animal experimentation studies have been trying to demonstrate mechanistic origins. Hypotheses that imply alterations towards fetal cortisol, insulin, IGF-1 or leptin metabolism have been suggested but only partially explain the fetal programming of metabolic diseases. Intriguingly, despite subtle modifications of the materno-fetal hormonal balance induced by experimentally induced intrauterine growth retardation (IUGR), the offspring exhibits dramatic perturbations of cellular stresses.
In addition, subsequent shifts in the transcriptional activity of DNA produce sustained metabolic adaptations. In tissues and organs controlling metabolic homeostasis (i.e. hypothalamus, adipose tissue, gut, heart), there are a number of phenotypes of differential energy metabolism induced by maternal nutrition. Critically, the observed alterations are consistently sustained by the modulation of genes controlling DNA methylation (e.g. FTO, DNMTs) and histone acetylation, strongly suggesting epigenetic programming. Additionally, the programmed phenotype by maternal nutrition is stable and reproducible, implying that specific targeted epigenetic alterations induced by the perinatal energy status have yet to be uncovered.


Neonatal overfeeding in mice predisposes to glucose intolerance to offspring (F1) and grand-offspring (F2) of over nourished individuals (F0) through the paternal lineage: Potential role of epigenetics

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Epidemiologic evidence suggests that sub-optimal nutrition during foetal and/or postnatal development influences diabetes risk later in life. In addition, such environmentally-induced phenotypes may manifest in subsequent generations, even when the environmental triggers are not present anymore (transgenerational effects). We have previously generated a mouse model of neonatal over-nutrition (ON-F0) by culling offspring to 4 pups per dam during lactation. Neonatal overfeeding led to rapid early weight gain and later development of metabolic syndrome in adult mice, by age 6 months: i.e. obesity, hyperglycaemia, hyperinsulinaemia, insulin resistance and glucose intolerance. Next, we aimed to explore whether neonatal over-nutrition may influence metabolism of successive generations, F1 and F2. Strikingly, we showed that impaired glucose tolerance and hyperglycaemia are inherited into the following generations F1 and F2 through the paternal lineage. Importantly, offspring (ON-F1) and grand-offspring (ON-F2) of neonatally overfed male mice (ON-F0) are not themselves overfed during lactation. Thus, transmission of the diabetic phenotype must occur through, nutritionally-induced, modifications in cells of the germ line. It has been proposed that trans-paternal inheritance of such environmentally-acquired phenotypes might be mediated, in part, by epigenetic mechanisms. In summary, we demonstrate that neonatal nutrition may influence metabolism of affected individuals (F0), their offspring (F1) and even their grand-offspring (F2).

Genomic Imprinting and Epigenetic Programming of Metabolic Disease

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Imprinted genes are important regulators of the balance between supply and demand systems that are crucial to fine-tune mammalian growth. The distinctive features of imprinted genes are their mono-allelic parental-specific expression and their selective roles in key mammalian physiological pathways related to maternal resource acquisition. Our studies using imprinted mouse models of fetal growth restriction have shown that placental materno-fetal transport of System A amino acids and calcium adapts according to fetal requirements of these nutrients. We also found that when placental supply exceeds fetal demand in overgrowth models, the large placentas respond to resource allocation signals and down regulate the nutrient transfer. Our latest work shows that imprinted genes play important roles in the control of endocrine functions of the placenta, with implications for maternal metabolism during pregnancy. These placental adaptations have marked effects on nutrient delivery to the fetus, resulting in programming an organism’s homeostatic mechanisms with metabolic consequences extending to adulthood. There is increasing evidence that epigenetics may underpin interactions between the genome and the environment. Environment-induced changes to the epigenome that occur during epigenetic programming may contribute to increased risk of diabetes in later life. These concepts will be illustrated by our studies on epigenetic regulation by early-diet and aging of the type 2 diabetes susceptibility gene Hnf4a.

Evidence that early growth influences adiposity at age 9-13 years and is mediated by epigenetic regulation of gene expression

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Early environmental events in postnatal life are postulated to cause aberrant epigenetic marking and precipitate altered expression of specific genes. This in turn may affect body composition and metabolic health in childhood. Participants were drawn from a nutritional intervention study of preterm infants carried out in early postnatal life. Blood and saliva samples were collected at age 9-13 years for DNA and RNA analysis. Up-regulation of gene expression in low thrive’ (n=12) versus high thrive children (n=12) was assessed. Thrive was determined by differences in z-scores for weight between term and term plus 12 weeks. Levels of DNA methylation at 7 CpG sites within TACSTD2 were analysed by Pyrosequencing. Methylation levels of TACSTD2 (mean across 7CpGs) in DNA extracted from saliva and blood (n=52) were closely correlated (rho=0.87, p<0.0001). However, methylation levels from saliva were considerably lower (mean % (SD) = 38.7 (15.4) compared to 68.9 (16.3)). TACSTD2 methylation was lower in low thrive individuals and was also associated with an increase in total body mass (kg) at age 9-13 years (blood p=0.012, saliva p=0.001). This latter association was driven by a reduction in fat mass; change in fat mass per percentage change in DNA methylation; blood -146.4g (95% CI -242.4, -50.3) p=0.004; saliva -149.3 (95% CI -235.2, -63.3) p=0.001. These results show an association between early growth, epigenetic regulation of gene expression and body composition in childhood.
Epigenetic regulation of beta-cell function
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The abnormal intrauterine milieu of intrauterine growth retardation (IUGR) permanently alters gene expression and function of pancreatic beta-cells leading to the development of diabetes in adulthood. Expression of the pancreatic homeobox transcription factor Pdx1 is permanently reduced in IUGR and epigenetic modifications are responsible for this decrease. Exendin-4 (Ex-4), a long-acting glucagon-like peptide 1 (GLP-1) analogue, given on days 1-6 of life increases Pdx1 expression and prevents the development of diabetes in the IUGR rat. Here we show that Ex-4 increases USF-1 and PCAF association at the proximal promoter of Pdx1, thereby increasing histone acetyl transferase (HAT) activity leading to a permanent increase in histone H3 acetylation and H3K4 methylation. Normalization of these histone modifications precludes DNA methylation thereby preventing silencing of Pdx1 in islets of IUGR animals. These studies demonstrate a novel mechanism whereby a short treatment course of Ex-4 in the newborn period prevents diabetes in adulthood by restoring Pdx1 promoter chromatin structure thus preserving Pdx1 transcription.

C.2: Maternal nutrition: impact on pregnancy outcomes

Impact of dietary factors in pregnancy on risk of pregnancy complications: results from the Norwegian MoBa cohort
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The Norwegian Mother and Child Cohort Study (MoBa) is a nationwide population-based pregnancy cohort study that between 1999 and 2008 has recruited 90,723 women with 106,981 pregnancies and 108,487 children. The objective of MoBa is to test specific aetiological hypotheses by estimating the association between exposures and diseases with special focus on disorders that may originate in early life. Maternal diet and nutritional status during pregnancy is an important determinant of maternal and foetal health and dietary factors are included in a many different sub studies as an exposure or a covariate. The pregnancy complications studied in MoBa so far are preeclampsia and preterm birth. In a study of preterm birth, defined as delivery before week 37, intake of fish twice a week or more was associated with lower risk than intake of fish less than twice a week B (relative risk 0.84; 95% confidence interval (CI): 0.74, 0.95). As to preeclampsia, results form MoBa suggest that vitamin D supplementation may reduce the risk in nulliparous women, with a 27% lower risk for women taking 10-15 µg/day as compared to no supplements (relative risk: 0.73, 95 % CI 0.58, 0.92). Furthermore, results from MoBa also suggested that adherence to a dietary pattern characterized by high intake of vegetables, plant foods and vegetable oil was associated with decreased risk of preeclampsia (relative risk for tertile highest versus lowest tertile scores: 0.72; 95% CI: 0.62, 0.85). Future studies will explore dietary risk factors and pregnancy complications in more depth.

Discordant secular trends in maternal body size and offspring birth weight of term births in France between 1972 and 2003
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OBJECTIVE: The weight of an infant at birth is associated with maternal anthropometry. We investigated secular trends in maternal weight before and during pregnancy and in infant birth weight in France, from 1972 to 2003. METHODS: Nationally representative perinatal surveys were conducted in France in 1972, 1981, 1995, 1998 and 2003. Information on maternal characteristics were collected by interview in the postpartum period and data on delivery and on the infant were extracted from hospital records. RESULTS: Maternal pre-pregnancy weight, height, body mass index and pregnancy weight gain all increased from 1972 to 2003; however birth weight did not show a continuous increase over the same period. When adjusted for gestational age and maternal smoking during pregnancy, mean birth weight increased between 1972 and 1995 but not afterwards reflecting an increase SGA and a decrease LGA births. The association between maternal anthropometry and birth weight was significantly weaker in 2003 than in 1972. The percentage of induced deliveries increased over the period, significantly more in overweight and obese women but further adjustment for type of delivery (induced or not) did not modify this downward trend of birth weight. CONCLUSION: In contrast with other countries, even if maternal size increased sharply between 1972 and 2003 in France, birth weight did not show a similar upward trend. Changes in French obstetric practices did not explain the observed downward trend in mean birth weight since 1995. Further research are needed to identify factors associated with this increasing trend in SGA births.

Impact of dietary factors on the risk of gestational diabetes: Review focusing on epidemiologic evidence
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Gestational diabetes mellitus (GDM), a common pregnancy complication, is a growing health concern. GDM has been related to substantial long-term adverse health outcomes for both mother and baby, including elevated risk for obesity, metabolic syndrome, cardiovascular disorders, and diabetes. Moreover, accumulating evidence from in vivo and animal studies demonstrated that maternal hyperglycaemia impairs embryogenesis as early as the pre-implantation stages of development. Collectively, these data underscore the significance of understanding risk factors for GDM and preventing GDM among high risk populations. This lecture...
will review epidemiological evidence on emerging novel modifiable risk factors that may contribute to the early prevention of GDM; in particular dietary factors that may be related to elevated GDM risk. The lecture will also raise major methodological concerns on available epidemiological studies of GDM risk factors. Pregnant women, or women planning pregnancy, are generally highly motivated to follow advice to improve the outcome of pregnancy, and hence pregnancy represents an ideal time in life to advocate for a healthy lifestyle.

High rate of overweight, obesity, dyslipidemia and hypertension in infants and children from mothers with gestational diabetes mellitus (GDM)

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Objective: Birth weight is one of the major determinants for the risk of infants from mothers with GDM to develop overweight, obesity and diabetes. The aim of this study was to investigate the correlation of birth weight with anthropometrics, metabolic parameters and blood pressure in early childhood. Methods: Up to now data from 242 children aged 8.5 years (2.0-14.0) were ascertained. We measured weight, length, blood pressure, serum levels of cholesterol and triglycerides (TG), insulin and glucose. Actual data were correlated with anthropometric data at birth. Results: 27.7% had a BMI >90th with 10.3% >97th, 13.2% <10th centile. Elevated TG (>110 mg/dl) or cholesterol (>160 mg/dl) was seen in 11.6% and 47.5%, respectively. 31% had a LDL/HDL ratio >2, 14% a HOMA ratio >2.5. Elevated systolic or diastolic blood pressure was seen in 31.9% and 4.9%, respectively. Children with a BMI >90th had significantly higher lipids and insulin resistance index than normal or underweight children. BMI-SDS was positively correlated with TG. BMI at birth was correlated with BMI-SDS at follow up. Children born LGA had the highest rate of BMI >90th, SGA the highest rate of underweight. Children born LGA had significantly higher TG and insulin resistance index compared to AGA or SGA. Conclusion: The preliminary analysis showed a high rate of BMI >90th and a high number of dyslipidemia and hypertension in overweight and obese children. Birth weight seems to affect growth pattern as well as lipid and glucose metabolism in childhood. Final results will be presented.

The role of oxidative stress and antioxidant supplementation in pregnancy disorders

Lucilla Poston
Division of Reproduction and Endocrinology, King’s College London, UK

Oxidative stress is widely implicated in reproductive performance including infertility, miscarriage, diabetes related congenital malformations and pre-eclampsia. Our research has focussed on the role of free radicals and antioxidant capacity in pre-eclampsia. Assessment by measurement of markers of lipid peroxidation or of antioxidant capacity has provided unequivocal evidence for oxidative stress in this disorder. Partial failure of the process of placentaion has been implicated, with recent evidence proposing that ischaemia reperfusion in the placenta may contribute to oxidative stress in trophoblast. Endoplasmic reticulum stress in the placenta may also play a role. Deficiency of selenium, which has been associated with pre-eclampsia, may also compromise antioxidant capacity through reduced activity of selenium dependent antioxidant enzymes eg glutathione peroxidase. We and others have performed large scale randomised controlled trials to determine whether early supplementation with vitamins C and E in women at risk of pre-eclampsia may be beneficial but these studies have shown no evidence for prevention of pre-eclampsia. Whether this represents the wrong antioxidant strategy or whether supplementation has been too late in pregnancy to be beneficial is not known. Maternal obesity is a strong risk factor for pre-eclampsia, and recently, in an animal model of maternal obesity we have found evidence of oxidative stress in the oocytes of obese animals prior to pregnancy as well as in early stage embryos. This adds to the growing evidence for a greater focus on the pre-conceptual period in prevention of pregnancy disorders including those related to oxidative stress.

A.3: Early origins of disease: research opportunities through new methods and integration

Drawing causal inferences in epidemiological studies of early life influences

Andy Ness, Alex Griffiths, Laura Howe, Sam Leary

Andy Ness Professor of Epidemiology, Sam Leary Lecturer in Statistics
Alex Griffiths Research Assistant, Department of Oral and Dental Science, University of Bristol
Laura Howe Research Associate, Department of Social Medicine, University of Bristol

Observational studies are can describe associations between early life exposures and subsequent outcomes in human populations. Drawing causal inferences from these associations is challenging as exposures often occur many years before the outcome and
are related to other early life exposures. An approach is required that combines traditional epidemiological and statistical principles with the use of novel or sophisticated analytic methods. To reduce bias in studies researchers conducting longitudinal studies of early origins researchers need to do all they can to reduce losses to follow up and to describe those that are lost to follow up. To avoid the play of chance researchers should concentrate on effect sizes and the strength of the evidence to support these effect sizes and they should be cautious in their interpretation of sub group analyses. More complex analytic approaches can and should be used to handle missing data and repeat measures. Addressing the issue of confounding is not straightforward. Statistical adjustment for the confounders measured in a study may help but lack of attenuation does not guarantee that the association is not confounded. Ecological studies, observational studies in populations with a different confounding structure and follow up of randomised trials (where these exist) can be informative. Genetic and non genetic instrumental variable approaches (such as Mendelian randomisation) may also provide causal insights. These approaches to confounding often require comparison of data from different populations or combination of studies to provide adequate power to provide robust estimates of the causal effect.

**Relation of Insulin-like Growth Factor-1 (IGF-1) to protein-induced kidney growth in healthy infants: results from a randomized clinical trial**

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5 Université Libre de Bruxelles, BRUSSELS, BELGIUM
6 University of Milan, MILAN, ITALY

Background: IGF-1 has been related to protein-induced kidney growth in animal models, but there is lack of data in healthy humans. Objective: To analyze the relationship of IGF-1 with protein-induced kidney growth in healthy infants. Methods: This multicenter European clinical trial (EU Childhood Obesity Project) examined 601 healthy 6-month-old formula-fed infants randomly assigned within the first 8 weeks of life (median 14 days) to receive an infant formula with higher or lower protein content (HP and LP, respectively). At age 6 months, a kidney ultrasound and anthropometry was performed, and a blood sample was collected (main outcome measures were kidney volume, weight, length and IGF-1 axis parameters). Results: The HP group had higher values than the LP group for kidney volume (cm3) (42.69.6 vs. 39.58.4, p<0.001), total IGF-1 (ng/ml) (58.3143.49 vs. 43.5334.47, p<0.001), free IGF-1 (ng/ml) (0.780.60 vs. 0.590.48, p<0.001) and IGFBP3 (ng/ml) (3023716 vs. 2974683, p<0.001), and lower levels than LP for IGFBP2 (ng/ml) (835364 vs. 1145416, p<0.001). Total and free IGF-1 correlated with weight (p<0.001), length (p<0.01), BMI (p<0.001) and kidney volume (r=0.140, p=0.01 for total IGF-1 and r=0.192, p=0.001 for free IGF-1). The linear regression models showed a significant independent effect of HP formula (β=2.30 (0.85, 3.75), p=0.002), free IGF-1 (β=0.24 (0.12, 0.36), p<0.001) and length (β=1.32 (1.00, 1.64), p<0.001) on kidney volume (β=0.23). Conclusions: IGF-1 could be a mediator of protein-induced kidney growth that may affect body size, kidney hyperplasia and kidney hypertrophy.
Breastfeeding and metabolic syndrome risk at 14 years: results from a pregnancy cohort study

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3 Centre for Developmental Health, Curtin University of Technology, PERTH, AUSTRALIA

Background: A shorter duration of breastfeeding in early infancy may be associated with an increased risk of the metabolic syndrome (MetS) in adolescence. Objective: To investigate associations between early infant feeding and prevalence of the MetS at 14 years as defined by three criteria in a prospective pregnancy cohort. Methods: Infant feeding history was assessed by parent/guardian questionnaire in 2420 children at one year of age participating in The Western Australian Pregnancy Cohort (Raine) Study. MetS was identified at 14 years using age-specific adolescent criteria from the International Diabetes Federation (IDF), the National Cholesterol Education Program Adult Treatment Panel III (ATP), and a population-derived ‘high-risk’ metabolic cluster variable. Results: MetS prevalence was 4.0% according to both IDF and ATP criteria while 26% were classified into the high-risk metabolic cluster. Breastfeeding cessation prior to two months of age was associated with an increased prevalence of the MetS at 14 years as defined by both IDF and ATP criteria (breastfed <2 months=7%; breastfed 2+ months=4%; p<0.05). In addition, breastfeeding cessation before two months was associated with high waist circumference as defined by IDF criteria at 14 years (OR: 1.79; 95% CI 1.39-2.31) and being in the high-risk metabolic cluster (OR 1.43; 95% CI: 1.12-1.82). Conclusion: This study supports the theory that a shorter duration of breastfeeding is associated with a higher prevalence of the MetS in adolescence.

This study was funded by a Heart Foundation/ Beyond Blue Strategic Research Initiative grant and NHMRC project grant # 403981.

Biomonitoring and biomarkers to unravel prenatal risk factors for later health outcomes

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An increasing number of studies address the concern that environmental pollutants may contribute to the early origin of diseases. Epidemiological studies suggest that prenatal exposure to air pollutants, several food contaminants, and chemicals present in consumer products are associated with adverse health effects which become manifest after birth. Changes in neurobehaviour, sexual development, the prevalence of asthma and allergy, increased cancer incidence and more recently changes in growth curves have been associated with pollutant exposure at early life stages. Experimental data support the role of developmental exposures to environmental chemicals for male and female reproductive dysfunctions, prostate, breast and uterine cancers, neurobehavioral problems and immune diseases. Animal data often use high doses and extrapolation of the outcomes to humans is not straightforward also due to differences in pregnancy physiology. Prospective human cohort studies are needed to demonstrate the relationship between early exposures and long term health effects. Few studies are yet available. It has been hypothesized that subtle effects induced by pollutant exposure during development can lead to functional deficits and altered programming leading to increased disease/dysfunction risk later in life. Biomarker analysis may provide sensitive tools to trace these subtle changes and obtain mechanistic insight in the causal pathway between external exposure and health effects in human population studies. Biomarkers of exposure can be measured in mother’s preconceptionally, during pregnancy or after birth. Different biological tissues such as peripheral or cord blood samples, hair samples, meconium, urine give specific information which reflect the actual dose during pregnancy or at birth. Biomarkers of effect may include changes in hormone levels, oxidative stress parameters, changes in gene expression levels, epigenetic changes.

B.3: Programming of bone health

Friday, May 7th 10.45 – 12.20

Insights into the programming of bone development from the ALSPAC cohort

JH Tobias

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This talk will review associations between several proxy measures of in utero nutrition, and total body bone mineral content (BMC), bone area (BA) and bone mineral density (BMD), as assessed at age 9.9 years in the Avon Longitudinal Study of Parents and Children (ALSPAC).

Birth weight in this cohort was positively related to BMC, BA and BMD. These associations were explained by co-association of birth weight with body size in later childhood, since they were completely attenuated by adjusting for height and weight. Indeed in height and weight adjusted analyses, an inverse association was observed between birth weight and BMD at age 9.9, suggesting that after relationships with bone and body size are taken into account, birth weight is actually a negative influence on bone mass. In analyses of associations between bone mass at age nine and background UVB during the third trimester of pregnancy (a proxy measure for maternal vitamin D status), maternal UVB was positively related to BMC, BA and BMD. After adjusting for height, which is related to maternal UVB exposure, these associations were only partially attenuated, suggesting that maternal UVB also affects skeletal size and mass independently of longitudinal growth, possibly by increasing periosteal expansion.

Maternal folate intake was positively related to BMD of the spine sub-region independently of body size. Although co-association with folate intake in childhood could explain this relationship, maternal MTHFR genotype affected spine BMD independently of child MTHFR genotype, suggesting that maternal folate status has an independent effect on bone development of the off-spring.
These results confirm that bone development in childhood is related to several proxy measures for nutritional status in utero. Although these associations were in part explained by co-association with body size, some of these relationships were size independent, suggesting possible effects on bone density.

**Bone quantitative ultrasound measurements in breastfed and formula fed infants**

*Francesco Savino, Serena Viola, Valentina Tarasco, Maria Maddalena Lupica, Elisa Petrucci, Roberto Oggero, Pier-Angelo Tovo*

Ospedale Infantile Regina Margherita, TORINO, ITALY

**Aim:** Nutritional status in infancy may have an impact in bone development. Breastfed infants not receiving supplemental vitamin D are at risk of rickets. The objective of this study was to assess the influence of kind of feeding and supplementation of vitamin D on metacarpal quantitative ultrasound (QUS) parameters in early life.

**Methods:** 103 healthy infants, 63 breast-fed (BF) and 40 formula-fed (FF), aged <12 months, underwent QUS evaluation with QUS DBM Sonic Aurora IGEA (MO, Italy), which measures speed of sound (mcSoS), index of bone tissue density, and bone transmission time (mcBTT), determined by cortical bone thickness. Z-scores for age and length were also considered.

**Results:** Median (range) QUS parameters in BF and FF infants were: mcSoS 1630 (1574-1672) vs 1646 (1620-1663) m/s, mcBTT 0.75 (0.46-1.04) vs 0.93 (0.72-1.12) s, Z-score SoS-age -1.19 (-4.2,+1.19) vs +0.38 (-1.83,+1.18), Z-score BTT-age -1 (-4.4,+1.52) vs +0.66 (-1.53,+2.99) e Z-score BTT-length -1.5 (-4.96,+1.51) vs +0.17 (-1.98,+2.01). We found a statistically significant difference (p<0.0001) between the two groups for all QUS measurements, with lower values in BF infants. BF not supplemented with vitamin D had lower ultrasound parameters than FF and BF receiving 400 UI of vitamin D (p<0.005).

**Conclusion:** In our research lower bone density measured in BF infants may be related to lower vitamin D content in breast milk than in formula. The higher ultrasound values observed in BF supplemented with vitamin D support this assumption, confirming beneficial effects of vitamin D on programming of bone health.

**Are early growth and nutrition related to bone health in adolescence?**

*Christian Molgaard, Anni Larnkjær, Alicja Budek, Kim F Michaelsen*

Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen, Denmark

**Background:** It is generally accepted that peak bone mass (PBM) is important for later fracture risk in elderly. In the Copenhagen Cohort Study (CCS) we have earlier shown that breastfed infants had significantly higher s-osteocalcin concentrations than formula fed infants. Furthermore, an inverse association between IGF-1 in infancy and adolescence at 17 y has been described in CCS. The relation between early nutrition, growth and later bone mass at 17 y, which is close to the age where PBM is achieved, is less clear.

**Objective:** To evaluate whether there are relations between early nutrition, early growth and later bone mass in adolescence.

**Design:** Participants in CCS were examined at 9 mo (n=143), and 17 y (n=109) with anthropometry, food registration and whole body DXA scanning (17 y only). Total body (T) and lumbar spine (LS) DXA values were used.

**Methods:** Sex adjusted T-bone mineral content (BMC) and T-bone area (BA) were positively correlated to growth in weight and length in the first 9 month (all p<0.04), weight at 9 mo (both p<0.004), but not birth weight. Protein and energy intake at 9 mo were not correlated to BMC or BA at 17 y, but were related to growth in weight and length. BMC and BA at 17 y was related to serum IGF-1 in infancy. BMC, BA and bone mineral density (BMD) at 17 y was related to birth weight and length. BMC, BA and BMD at 17 y was positively correlated to birth weight (all p<0.04) and negatively correlated to birth length (p<0.04). BMC, BA and BMD at 17 y was positively correlated to protein intake (all p<0.04) and negatively correlated to energy intake (all p<0.04). BMC, BA and BMD at 17 y was positively correlated to protein and energy intake during the first 9 month (all p<0.04) and negatively correlated to energy intake during the last 3 month (all p<0.04).

**Results:** Sex adjusted T-bone mineral content (BMC) and T-bone area (BA) were positively correlated to growth in weight and length in the first 9 month (all p<0.04), weight at 9 mo (both p<0.004), but not birth weight. Protein and energy intake at 9 mo were not correlated to BMC or BA at 17 y, but were related to growth in weight and length. BMC and BA at 17 y was related to serum IGF-1 in infancy. BMC, BA and bone mineral density (BMD) at 17 y was related to birth weight and length. BMC, BA and BMD at 17 y was positively correlated to birth weight (all p<0.04) and negatively correlated to birth length (p<0.04). BMC, BA and BMD at 17 y was positively correlated to protein intake (all p<0.04) and negatively correlated to energy intake (all p<0.04). BMC, BA and BMD at 17 y was positively correlated to protein and energy intake during the first 9 month (all p<0.04) and negatively correlated to energy intake during the last 3 month (all p<0.04).

**Conclusion:** As shown by others early body size and growth in infancy is related to later bone mass. Furthermore duration of exclusive breast feeding seems to be positive related to later spinal bone mass. We speculate if the mechanism could be related to early influence on bone turn-over.

**Insufficient Dietary Vitamin D Intake amongst Pregnant Women in Ireland**

*Ciara McGowan, Jacinta Byrne, Jennifer Walsh, Mick Foley, Rhona Mahony, Fionnuala McAuliffe*

University College Dublin, DUBLIN 2, IRELAND

Maternal vitamin D status during pregnancy is essential for ensuring normal fetal skeletal growth. Low maternal vitamin D status is associated with reduced intrauterine long bone growth and lower infant birth weight as well as poor bone mineralisation in childhood. Severe maternal deficiency can result in rickets in the offspring. Previous research in an Irish cohort showed that dietary intakes of vitamin D are significantly below recommended levels. Low dietary intakes coupled with northern latitude (40-60N) increase the risk of poor maternal vitamin D status of pregnant women in Ireland. The aim of this study was to determine dietary vitamin D intakes in an Irish obstetric cohort. 44 healthy pregnant women were recruited from an antenatal clinic at the National Maternity Hospital, Dublin. Women included in the study were over 18 years of age, were not taking supplements containing vitamin D and had adequate English. All participants completed a 3 day food diary during each trimester of pregnancy. Collected data were entered into NetWISP (version 3.0) (Tinuviel Software, Llanfechell, Anglesey, UK) and analysed using SPSS (version 15.0) (SPSS Inc, Chicago, IL, USA). Mean intakes of vitamin D were 2.41g/day, 2.44g/day, and 2.61g/day during the 1st, 2nd and 3rd trimesters respectively. Alarmingly, only 2 women met the current vitamin D recommendations in Ireland. These data highlight the need for strategies to increase vitamin D intakes amongst pregnant women in Ireland. Mandatory vitamin D supplementation during pregnancy and fortification of foods with vitamin D may be necessary to achieve optimum maternal status.
PARALLEL SESSIONS

Does early nutrition program later bone health in preterm infants?
Mary Fewtrell, Childhood Nutrition Research Centre, UCL Institute of Child Health, London.

Preterm infants are at risk of metabolic bone disease (MBD) due to inadequate mineral intake. Although frequently asymptomatic during the neonatal period, we previously reported that MBD predicted reduced linear growth in infancy and mid-childhood. Nevertheless, some studies suggest that preterm infants undergo catch-up in bone mineralisation during infancy.

To examine the hypothesis that early nutrition programmes later bone health and peak bone mass, we studied 20 year old subjects who were born preterm and randomised to diet during the neonatal period; diets used varied markedly in nutrient and mineral content, and phosphate supplements were not provided. Despite large variations in early nutrient and mineral intake (and occurrence of MBD) during the neonatal period, randomised infant diet did not influence peak bone mass or turnover. However, the proportion of (unsupplemented) human milk in the neonatal diet was significantly positively associated with later whole body bone size and mineral content. Compared to population reference data, preterm subjects were significantly shorter with lower lumbar spine bone mineral density; deficits were greatest in those born SGA with birth weight <1250g.

The lack of effect of randomised infant diet on peak bone mass suggests that the observed deficits in height and lumbar spine bone mass may not be related to sub-optimal early nutrient or mineral intake. The higher whole body bone mass associated with human milk intake, despite its very low nutrient content, may instead reflect non-nutritive factors in breast milk. These findings are relevant to discussions on the mineral requirements of preterm infants.

C.3: Programming of neurodevelopment

The role of meta-analysis in the evaluation of the effects of nutrition on mental and motor development in children
Hania Szajewska, MD, The Medical University of Warsaw, Poland, hania@ipgate.pl

Recently, three systematic reviews (some with a meta-analysis) evaluated the effects of nutritional interventions such as iron, folic acid, or n-3 long-chain polyunsaturated fatty acids (LCPUFA) supplementation during pregnancy and/or in early life on the mental performance and psychomotor development of children. All reviews included randomized controlled trials (RCTs) only and involved searches of at least the Cochrane Library, MEDLINE, and EMBASE. Limited available evidence suggests that iron supplementation of infants may positively influence children's psychomotor development, while it does not seem to alter their mental development or behaviour (AJCN 2010 accepted for publication). Evidence from RCTs does not demonstrate a clear and consistent benefit of LCPUFA supplementation during pregnancy and/or lactation on child neurodevelopment and visual acuity (submitted). The use of multivitamin-containing folic acid supplementation during pregnancy does not benefit the mental performance of children (submitted).

These systematic reviews of RCTs have strengths and potential limitations. The inclusion of RCTs only could be considered the major strength. Randomization is the only means of controlling for unknown and unmeasured differences between comparison groups as well as those that are known and measured. Still, even if only RCTs are included, the reviews are not free of potential biases. Potential limitations relate to both the methodological quality of the included trials as well as the variations in the study populations, duration and amount of supplementation, outcome measures, and the times of outcome assessment.

In summary, the systematic review (with or without a meta-analysis) of RCTs is the principle research method used to evaluate medical interventions. However, an understanding of the strengths and limitations of this approach is needed by everyone involved in the decision making regarding the interventions assessed by this approach.

Folate intake in pregnancy and psychomotor development at 18 months
Charlotta Granström 1, Susanne Petersen 1, Marin Stram 1, Thorhallur Halldorsson 2, Emily Oken 3, Sjurdur Olsen 1
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2 Faculty of Food Science and Nutrition, School of Health Sciences, Univ Iceland, REYKJAVIK, ICELAND
3 Department of Population Medicine, Harvard Medical School, BOSTON, UNITED STATES OF AMERICA

Background: Studies in mice have suggested that folate deficiency in pregnancy may affect progenitor cells in fetal forebrain negatively whereas human trials have shown that maternal folate supplementation can prevent neural tube defects. We studied the association between maternal folate intake and psychomotor development at 18 months.

Setting: We studied 34649 children born to mothers participating in the Danish National Birth Cohort. Intake of dietary folate and folic acid from supplements was assessed by a 360-item food frequency questionnaire in mid-pregnancy. Dietary folate was partitioned into food sources. Mothers reported child development by standardized interview, which we used to generate child developmental scores (CDSs) at 18 months. We used multivariable cumulative ordinal logistic regression to evaluate the odds of higher CDSs associated with maternal folate intake, adjusted for confounders.

Results: Higher maternal dietary folate intake was associated with higher CDSs (odds ratio 0.69 [95% CI: 0.65, 0.74] for the highest vs. the lowest quintile of folate), whereas higher folic acid from supplements was not (odds ratio 1.02 [95% CI: 0.93, 1.11] for the highest vs. the lowest quintile of folic acid from supplements). Dietary folate from onion, tomatoes, and green leafy vegetables was associated with higher CDSs, whereas folate deriving from grain, dairy, and egg was not.

Conclusion: The associations observed between maternal dietary folate and early psychomotor development are unlikely to reflect an effect of folate itself but may instead be attributed to some food constituent(s), which coexist with folate in specific vegetables and fruit.
Prenatal and early postnatal fatty acid status and neurodevelopmental outcome at school age

Mija Hadders-Algra MD, PhD, Hedwig Kikkert, MSc, Corina de Jong, MSc

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Long-chain polyunsaturated fatty acids (LCPUFA) are essential components of the central nervous system. Quantitatively the most important LCPUFA are docosahexaenoic acid (DHA, omega-3) and arachidonic acid (AA, omega-6). Limited data is available on the association between prenatal LCPUFA status and long-term neurodevelopmental outcome. Systematic reviews on postnatal LCPUFA-supplementation indicated that supplementation with ≥ 0.30% DHA has a beneficial effect on neurodevelopment of term infants until 4 months. No consistent positive effect of LCPUFA-supplementation after early infancy has been reported.

Recently we carried out a prospective, double-blind, randomized control study in two groups of healthy term infants: a control group with standard formula (CF, n=169) and a LCPUFA-supplemented group (LF, n=146). A breastfed group (BF; n=159) served as a reference. Neurodevelopmental outcome was assessed at nine years in 72% of the original groups. LCPUFA supplementation did not affect neurological condition at nine, but it had an effect on cognitive function. The effect depended on presence or absence of maternal smoking during pregnancy. In children exposed to smoking LF was associated with better cognitive function, in children not exposed to smoking LF was associated with worse cognitive function. Children who were breastfed had a slightly but significantly better neurological and cognitive condition than formula fed children. Analysis of associations between neonatal fatty acid status and developmental outcome revealed a complex picture.

The data indicate that our understanding of relationships between early nutrition and long-term neurodevelopmental outcome is limited, most likely because the complex systems ‘nutrition’ and ‘nervous system’ preclude simple one-to-one relationships.

The study is part of the Early Nutrition Programming Project (EARNEST), which is funded under the Food Quality and Safety Priority of the Sixth Framework Programme for Research and Technical Development of the European Community (FOOD-CT-2005-007036, www.metabolic-programming.org).

Maternal intake of fish and docosahexaenoic acid during pregnancy and IQ of offspring measured at 5 years

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Long-chain polyunsaturated fatty acid (PUFA) supplementation has shown beneficial effects on neurodevelopment early in life. We explored the associations between maternal intake of fish and the particular long-chain n-3 PUFA: docosahexaenoic acid (DHA) and the general intellectual ability (IQ) of the offspring at 5y. Data derived from The Lifestyle During Pregnancy Study, which consists of 1783 mother-child pairs sampled from the Danish National Birth Cohort (n=101,042) based on maternal alcohol intake, diet and breastfeeding.

Measurements of maternal and offspring IQ were part of a comprehensive assessment of neurobehavioural development when the children were 5 years old. Fish intake was assessed in mid-pregnancy by an FFQ, and in gestation weeks 12 and 30 by telephone interviews. Women consistently reporting the same frequencies of fish intake in both interviews (n=708) were divided into quintiles of fish and DHA intakes quantified based on standard portion sizes and food tables.

Maternal fish intake was positively associated with IQ of the child, with an IQ increment of 0.98 points for each quintile of intake (95%CI 0.32-1.64), but this was attenuated after adjustment for a range of potential confounders including maternal IQ (increment 0.58, 95%CI: -0.04-1.20). Intake of DHA was more strongly associated with offspring IQ (increment for quintile 1.08, 95%CI: 0.42-1.74), and the association persisted after adjustment, even if the difference in IQ was attenuated (increment 0.62 95%CI: 0.01-1.23). Our data are compatible with a moderate positive association between dietary intake of DHA during pregnancy and intellectual ability of the offspring early in childhood.

Programming Neurodevelopment: The NUHEAL follow-up study

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Long chain polyunsaturated fatty acids (LC-PUFA) have essential functional and structural roles in the human body. Docosahexaenoic acid (DHA) is the most abundant LC-PUFA in mammalian brain. Some observational and interventional studies have reported beneficial effects of DHA on neurological development but information on long term effects of DHA supplementation during pregnancy is scarce. In order to assess the effects of DHA supplementation to expecting women on neurological development of their children, a multicenter, randomized, double blind, controlled trial was conducted. Healthy pregnant women from three European centres (Spain, Germany and Hungary) were randomly assigned to receive daily from 20 week of gestation till delivery a dietary supplement consisting of fish oil (FO) [500 mg DHA + 150 mg eicosapentaenoic acid], 400 μg 5-Methyltetrahydrofolate, both or placebo. Fatty acid levels in plasma and erythrocyte phospholipids (PLs) were determined in maternal blood at the 20th and the 30th week of pregnancy and at delivery as well as in cord blood. To assess neurological outcome the Hempel neurological examination
for toddler age and the Touwen Infant Neurological Examination (TINE) were performed at the age of 4 and 5½ respectively. Neurological condition was summarized as a clinical classification and a neurological optimality score (NOS) and fluency score. There were no significant differences among intervention groups with respect to the NOS, the fluency scores or the incidence of minor neurological dysfunction (MND), neither at 4 not at 5½ years of age. Likewise, there were no statistical differences in the Kaufman-ABC scores at 6 ½ years of age between intervention groups. In addition, a significant association between the occurrence of optimality (NOS=83) at 5 ½ and the levels of DHA in cord plasma and erythrocyte PLs [Plasma: Exp B IC 95% 1.101-2.275, P=0.013; phosphatidylethanolamine (PE): Exp B IC 95%1.200-4.347, P=0.012, phosphatidylcholine (PC): Exp B 1.071-3.492, P=0.029] was observed. Our results showed no beneficial effects of maternal FO supplementation during pregnancy on long term cognitive development of their children. However, higher DHA levels in cord blood were associated with a better neurological outcome in the children at 5 ½ years of age.

*This study is part of the EARNEST FP6 EU Project – FOOD-CT-2005-007036.

A.4: Perinatal life and diabetes risk

Friday, May 7th, 14.30 – 16.05

Early nutrition and risk of type 1 diabetes – experiences from the TRIGR study

Mikael Knip, Suvi Virtanen, and Hans K. Åkerblom

Short breastfeeding and early exposure to complex dietary proteins, such as cow’s milk proteins (the commonest weaning food) and cereals or to fruits, berries and roots have been implicated as risk factors for beta-cell autoimmunity and/or clinical T1D. TRIGR (Trial to Reduce IDDM in the Genetically at Risk) is an international randomized double-blind controlled intervention trial, designed to answer the question whether weaning to a highly hydrolyzed formula in infancy will reduce the risk of T1D later in childhood. The trial is running in 77 centers in 15 countries. TRIGR recruited initially 5606 newborn infants with a family member affected by T1D and enrolled 2160 eligible subjects carrying a risk-conferring HLA genotype. All recruited mothers were encouraged to breast-feed. The intervention lasted for 6-8 months with a minimum study formula exposure time of 2 months, and hydrolyzed casein and standard cow’s milk based weaning formulas were compared. 80 % of the participants were exposed to the study formula. The overall retention rate over the first 5 years is 86% and protocol compliance 94%. The randomization code will be opened when the last recruited child turns 10 years of age, i.e. in 2017. In our pilot study, weaning to a highly hydrolyzed formula reduced the cumulative incidence of one or more autoantibodies by a mean age 4.7 years. A recent follow-up analysis to age 10 years showed that this early nutritional intervention significantly decreased the appearance of both ≥ one and ≥ two autoantibodies after adjustment for the duration of study formula exposure.

The influence of maternal nutrient restriction in late pregnancy and accelerated postnatal growth on plasma insulin and leptin and hypothalamic gene expression following obesity in the sheep

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Objectives: Prenatal caloric restriction followed by accelerated postnatal growth influences later risk for metabolic diseases associated with obesity, raising the question as to whether long term programming of hypothalamic appetite control may be modulated by perinatal growth.

Methods: Pregnant twin-bearing sheep were either fed to requirements (R; n=8) or nutrient restricted to 60% of this amount (N; n=15) from 110 days up to term (~147 days). Twin offspring were reared to promote either accelerated (A) (RA, n=8; NA n=8) or standard (S) (NS, n=7) early postnatal growth. After weaning, offspring were then kept in a low activity environment until 17 months of age when insulin response to a GTT was assessed and entire hypothalami dissected for gene expression analysis by real-time PCR.

Results: Adult offspring body weight and composition were similar. Plasma leptin and insulin responsiveness were higher in N compared to R offspring. Whilst gene expression of hormone receptors i.e. insulin, leptin and ghrelin were unaffected, genes involved in insulin and leptin signalling (PTP1B), energy sensing (mTOR, AMPK, FTO), blood pressure regulation (AVP) and the glucocorticoid system (GCR) were overexpressed in N compared to R offspring.

Conclusions: Although maternal diet did not alter adult body weight or composition, long term systemic changes in leptin and insulin regulation were induced by fetal growth restriction. These adaptations were further associated with differential responses in the gene expression profiles within the hypothalamus, suggesting programmed alterations in energy sensing pathways.

Long term appetite regulation and metabolic effects observed in low birth weight rats reared artificially on a high protein milk formula

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High protein milk formulas are routinely used in infants born with a low birth weight to enhance growth. However indirect evidence points to a link between a high protein intake during early life and the prevalence of obesity in later life. We hypothesized that high protein milk supplementation to low birth weight pups during early postnatal life would impact hypothalamic appetite neuronal pathways development and have long lasting effects on feeding behaviour and on glucose and fat metabolism.
Rat pups born with a low birth weight were equipped with gastrostomy tubes on the 5th day of life. They received a milk formula with either a ‘normal’ (NP: 8.7 g protein/dL, n = 14), or a ‘high’ protein content (HP: 13.0 g/dL, n = 14), and were subsequently weaned to a standard, solid diet. The milk formula was without effect on neuronal projections emanating from the arcuate nucleus demonstrated by estimation of immunoreactive agouti-related protein and a-melanocyte-stimulating hormone fibres. Compared with rats that had received NP milk in the suckling period, rats that had been fed HP milk during pre-weaning period developed significant overweight from puberty through adulthood. The difference was associated with an increase in food intake, higher serum insulin, an increase in -cell number, a rise in plasma triglycerides and higher serum leptin correlated with an increased mesenteric fat mass with larger adipocytes. Concerning feeding behaviour, rats that have been fed HP or NP milk exhibited differences in the satiety period, resting postprandial duration and nocturnal meal pattern.

Maternal malnutrition programmes a prediabetic phenotype in the progeny

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Type 2 diabetes arises when the endocrine pancreas fails to secrete sufficient insulin to cope with the metabolic demand because of beta-cell secretory dysfunction and/or decreased beta-cell mass. Epidemiological studies have revealed strong relationships between poor foetal and early postnatal nutrition and susceptibility to diabetes later in life. Animal models have been established and studies have demonstrated that reduction in the availability of nutrients during foetal development programmes the endocrine pancreas and insulin-sensitive tissues. We have investigated several mode of early malnutrition in rats. Whatever the type of diet investigated, whether there is deficit in calories or protein in food, or even in presence of a high fat diet, malnourished pups are born with a defect in their beta-cell population with less beta-cell that do not secrete enough insulin and that are more vulnerable to the oxidative stress, and such population of beta-cell will never completely recover. Despite the similar endpoint, the cellular and physiological mechanisms that have contributed to the beta-cell mass alteration are different depending on the nature of the nutritional insult. Hormones operative during foetal life like insulin itself, insulin-like growth factors and glucocorticoids, as well as specific molecules like taurine, or islet vascularisation are implicated as possible factors amplifying the defect. The molecular mechanisms responsible for intrauterine programming of the beta-cells are still elusive, but amongst them, the programming of mitochondria could be a strong central candidate.

B.4: Dietary practice in mother and infants

Friday, May 7th, 14.30 – 16.05

Dietary patterns during pregnancy across Europe

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Background: Despite growing evidence that maternal diet during pregnancy may influence children’s long-term health, including effects on neurodevelopment, asthma and allergy, little is known about prevailing patterns and predictors of intakes in industrialized countries.

Methods: Existing projects in 14 European countries participated in this collaborative effort to characterize diet during pregnancy. Intakes of fruits/vegetables, meats and seafood were estimated using food group definitions standardized to maximize comparability, using the median and 25th/75th percentiles to compare consumption patterns across countries. Reported intakes were stratified by maternal smoking during pregnancy, age, education, and pre-pregnancy weight status.

Results: Intake disparities associated with maternal characteristics were widespread. Smokers (9-27% prevalence) reported lower intakes of fruits/vegetables in virtually all countries, as well as higher intakes of red/processed meats and lower intakes of seafood in numerous settings. Women >35y (6-28%) frequently reported higher fruit/vegetable, lower red/processed meat, and higher seafood intakes. More educated women frequently reported lower red/processed meats and higher seafood intakes. More educated women also reported higher intakes of fruits and vegetables in most countries, with the notable exception of Mediterranean countries, where intakes were markedly higher across all education levels. Pre-pregnancy overweight (18-41%) was less strongly associated with intake disparities.

Conclusions: Diet quality was markedly poorer among women who smoked during pregnancy, as well as among younger and less educated women. As these factors are associated with poorer reproductive outcomes, findings suggest potential benefits of targeting nutrition interventions to women readily identified by these characteristics as a means to address reproductive health inequalities.

Formula feeding is associated with weight gain in early infancy

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Introduction: Rapid weight gain in infancy is an important predictor of obesity in later childhood. Our aim was to determine which modifiable variables (demographic, infant feeding) are associated with weight gain in early life. Methods: Subjects were healthy term infants enrolled in NOURISH, a randomised trial evaluating an intervention to promote positive early feeding practices. The infants were weighed at birth and again at assessment which occurred when they were aged 3-6 months and before randomisation. Infant feeding practices and demographic variables were collected by questionnaire. Weight gain was defined as an increase in weight Z-
score (WHO standards) from birth to assessment indicating tracking above weight percentile. Variables associated with weight gain were evaluated using a logistic regression model.

Results: Complete data from 630 infants (90% of the total sample) with a mean age of 4.29 (SD 0.97) months were available. Bivariate analysis showed that only formula feeding and male gender were associated with a positive difference in weight Z-score between birth and assessment. After adjusting for mother’s weight status and age, infant’s birth weight, age and introduction of solid foods, the only variable associated significantly with weight gain was formula feeding [OR=1.97 (95%CI 1.30-2.98), P=0.001].

Conclusion: This analysis supports the contention that there is an association between formula feeding and weight gain in the first months of life. Mechanisms may include the higher protein intake and increased risk of overfeeding related to maternal regulation of volume associated with formula feeding.

**Influence of parental attitudes in the development of children dietary practice**

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Parental feeding styles were linked to child nutritional behaviour in cross-sectional studies. Revision of available data on effects of parental feeding attitudes and styles. The development of children’s food preferences involves a complex interplay of innate, familial and environmental factors. Parents employ a variety of strategies to influence children’s eating habits some of which are counter-productive. Over-control, restriction, pressure to eat, promise of rewards to children have negative effects on food acceptance. Parents’ food preferences and eating together provide an opportunity to model good eating habits. Parents should be informed that repeated taste exposure can reduce neophobia and increase acceptance of healthy foods. Effective prevention programs must focus on providing anticipatory guidance on parenting to foster patterns of preference and food selection in children more consistent with healthy diets and promote children's ability to self-regulate intake. Guidance for parents should include information on how children develop patterns of food intake in the family context. Practical advice for parents includes how to encourage children’s preferences for healthy foods and how to promote acceptance of new foods by children. Parents need to understand the costs of coercive feeding practices and be given alternatives to restricting food and pressuring children to eat. Providing parents with easy-to-use information regarding appropriate portion sizes for children is also essential as are suggestions on the timing and frequency of meals.

A positive parental role model may be a better method for improving a child’s diet than attempts at dietary control.

**Dietary patterns during pregnancy and the risk of postpartum depression**

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Background: Research on the relationship between diet in pregnancy and postpartum depression (PPD) has focused on individual nutrients and foods rather than dietary patterns. We examined in a population-based cohort in Greece whether dietary patterns in pregnancy are related to postpartum depression. Methods: The study used data prospectively collected from women participating in the mother-child cohort study (‘Rhea study’) in Crete, Greece 2007-2009 (n=529). Dietary intake during pregnancy was assessed by food frequency questionnaires completed with a personal interview in mid-pregnancy. Factor analysis was used to explore dietary patterns in pregnant women. Women were classified into ‘Western’, ‘Intermediate’, and ‘Health conscious’ diet groups. The Edinburg Postpartum Depression Scale (EPDS) was used to assess PPD symptoms. Associations between maternal dietary patterns in pregnancy and PPD symptoms were investigated by multivariable regression models after adjusting for confounders.

Results: The prevalence of high levels of PPD symptoms was 14%. EPDS was negatively associated with adherence to a healthy conscious dietary pattern (coefficient -1.73, p=0.027) during pregnancy. Olive oil intake (>40-g/day) was associated with low levels of PPD symptoms (OR, 0.57; 95% CI, 0.35-0.94). Unadjusted and adjusted analyses showed that women in the ‘Intermediate’ or the ‘Health Conscious’ class were about 50% less likely to have high levels of PPD symptoms compared with those who followed a western type diet.

Conclusion: These finding indicate that a dietary pattern based on vegetables, fruits, pulses, nuts, dairy products, fish, and olive oil, was associated with reduced risk for postpartum depression.

**Introduction of complementary feeding in 5 European countries – recommendations vs. implementation**

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Little information is available on the practice of introducing complementary feeding across Europe. We report on the times of complementary feeding introduction and effects of energy providing liquids (EPL) in healthy infants in five European countries.

Methods: Between October 2002 and June 2004, healthy, singleton, term infants fed either breast milk (BF) for at least 3 completed
months (n=588) or study formula (FF) (n=1090) with different protein contents were recruited. Three-day-weighed food protocols were obtained at ages 1 to 9 and 12 completed months.

At the age of 4 completed months, already 37% of FF infants and 17% of BF infants consumed solids and 43% of FF infants and 13% of BF infants consumed EPL. FF infants with EPL intake had a significant lower intake of formula milk (age 2 to 5 months p<0.05) and solids (age 7 to 9 and 12 months p<0.05). We found significant differences between the countries, with the highest proportion of infants with solid intake in Belgium (FF infants 56%, BF infants 43%) and the highest proportion of infants with EPL intake in Poland (FF infants 87%, BF infants 18%) at the age of 4 months. Multiple regression showed the country of residence as the strongest predictor of time of complementary feeding introduction.

Solids and EPL were introduced earlier than recommended to a high proportion of infants, particularly FF infants. Country of residence strongly influenced the time of introduction of complementary feeding, which should lead to adapted strategies for counseling parents.

C.4: Environmental toxicants and programming

The OBELIX project: prenatal exposure to endocrine disruptors and obesity

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The European research project ‘OBesogenic Endocrine disrupting chemicals (EDCs): Linking prenatal eXposure to the develop-ment of obesity later in life’ (OBELIX) will test the hypothesis whether early exposure to EDCs may be a risk factor for obesity and related metabolic diseases later in life. OBELIX is a four-year project which started in May, 2009 and has following five main objectives: 1) To assess prenatal exposure in humans to major classes of EDCs identified as potential inducers of obesity (i.e. dioxin-like compounds, non- dioxin-like polychlorinated biphenyls, organochlorine pesticides, brominated flame retardants, phthalates and perfluorinated compounds) using mother-child cohorts from four European regions with different food contaminant exposure patterns; 2) To relate early life exposure to EDCs with clinical markers, novel biomarkers and health effect data related to obesity; 3) To perform hazard characterization of in utero exposure to EDCs for the development of obesity later in life, using a rodent model; 4) To determine mechanisms of action of obesogenic EDCs on developmental programming with in vivo and in vitro genomics and epigenetic analysis; and, 5) to perform risk assessment of prenatal exposure to obesogenic EDCs in food, by integrating maternal exposure through food, contaminant exposure and health effect data in children, and hazard data in animal studies. This project has received funding from the European Community’s Seventh Framework Programme [FP7/2007-2013] under grant agreement OBELIX n° 227391.

Cohort Study on Infant Atopic Dermatitis and Fetal Exposure to Persistent Organic Pollutants (POPs), Heavy Metals and Brominated Flame Retardants (BFRs)

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Our previous studies revealed that Japanese fetuses were exposed to several persistent organic pollutants (POPs), heavy metals and brominated flame retardants (BFRs). In Japan, rapid increase of allergic diseases such as atopic dermatitis (AD) and asthma among children has been reported. To investigate the association between fetal exposure to POPs, heavy metals and BFRs and allergic diseases among the infants, we collected 105 umbilical cords in Chiba City (Japan). Following the sampling of umbilical cords, we conducted questionnaire survey of infants about the occurrence of AD at 7-months old. We measured concentrations of organochlorines (polychlorinated biphenyls [PCBs], -hexachlorocyclohexane [HCH], p,p'-DDTs, p,p'-DDE, nonachlor, oxychlordane, hexachlorobenzene [HCB], mirex), heavy metals (Hg, Cd, Pb) and BFRs including polybrominated diphenyl ethers (PBDEs). This study was approved by the ‘Congress of Medical Bioethics’ of Chiba University. Our results indicated an association between the fetal exposure to PCBs and HCH and the occurrence of AD in Japanese infants. PCB concentrations in umbilical cords of AD group (n=30) were 6846 pg/g-wet weight (mean±S.D.), non-AD group (n=58) were 5731 pg/g-wet weight, and HCH concentrations were 108 117 pg/g-wet weight and 62 42 pg/g-wet weight, respectively. Odds ratio were significant at 120 pg/g-wet weight for PCBs and 40 pg/g-wet weight for HCH, respectively. However, there are still some uncertainties such as it was not clear if the association was because of combined effects of several chemicals or the occurrence of AD was because of the fetal exposure or through breast milk exposure.
Research on environmental toxicants in the Norwegian HUMIS cohort

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The “Norwegian Human Milk Study” (HUMIS), is a multi-center cohort of Norwegian mothers who have recently given birth and their babies. More than 2000 mothers have been recruited to date. The overall aim is to study health effects of pre- and postnatal exposure to environmental toxicants. Since persistent organic pollutants have very long half lives, the levels measured in human milk will reflect intrauterine exposure as well as postnatal exposure.

We will present the results from two studies:

1) We have studied the association between the toxicant Hexachlorobenzene (HCB) and the risk of being born “small for gestational age” (SGA). Details concerning this study have already been published and the results will only be shortly summarized. Being among the 10% highest exposed, compared to among the 10% lowest exposed to HCB, increased the risk of being born SGA, two- to three-fold in our study. The association was restricted to infants of past or current smokers.

2) Experimental studies have indicated that toxicants belonging to the group of Brominated flame retardants (BFRs), may interfere with thyroid hormone homeostasis. Intrauterine exposure is of particular concern due to the susceptibility of the fetal brain to alterations in thyroid hormones. Few human studies exist. BFRs were measured in milk samples from a subset of 239 women and TSH was measured in babies three days after delivery as part of the Norwegian screening program. We observed no statistically significant associations between TSH and the polybrominated diphenyl ethers: BDE 209, 47, 99, 153, 154, 209 and HBCD.

Non-teratogenic environmental toxicant exposure of organogenesis stage embryos results in osteoporotic bones in adults

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By now considerable evidence has been accumulated implicating maternal malnutrition during pregnancy in the etiology of age-related osteoporosis. We chose to explore whether in utero exposure to environmental toxicants may also lead to a deteriorated bone remodelling in adults. Pregnant ICR mice were exposed to a single injection of 5-Aza-2-Deoxycytidine (5-AZA) at a dose of 0.15mg/kg in the middle of organogenesis (day 10 of pregnancy). Neither excessive cell death in limb buds of embryos tested 24 hours after 5-AZA injection nor external and skeletal anomalies in newborns were observed. Yet, micro-CT scanning revealed that femora of 5-month old male offspring had a significantly decreased bone mineral density and injured trabecular microarchitecture. Furthermore, we observed that offspring of 5-AZA treated mice were more sensitive than control offspring to postnatal chronic mild stress-induced bone loss. Finally, searching for potential mechanisms underlying the phenomenon we observed that the expression of some microRNAs, which are able to regulate the expression of key osteoblastogenic and osteoclastogenic genes such as Runx2, Smad 5 and M-CSF is altered in the hind limb buds of embryos of 5-AZA exposed mice. Collectively, these results demonstrate for the first time that exposure of organogenesis stage embryos to environmental toxicants at non-teratogenic dose levels can induce bone loss in adults and allow hypothesizing a pathway underlying this pathology.

Developmental exposure to endocrine disruptors and the obesity epidemic

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Many chemicals in the environment, in particular those with estrogenic activity, can disrupt the programming of endocrine signalling pathways that are established during development and result in adverse consequences that may not be apparent until much later in life. Most recently, obesity and diabetes join the growing list of adverse consequences that have been associated with developmental exposure to environmental estrogens during critical stages of differentiation. These diseases have quickly become significant public health issues and are fast reaching epidemic proportions worldwide. Many experimental animal studies document an association of exposure to environmental estrogens and the development of obesity. For example, an animal model of perinatal exposure to diethylstilbestrol (DES) has proven useful in studying mechanisms involved in abnormal programming of various differentiating estrogen- target tissues including adipocytes. Other examples of environmental estrogens, including the phytoestrogen genistein and the environmental contaminant Bisphenol A, have also been linked to obesity later in life. Epidemiology studies support similar findings in humans. Together, these data suggest new targets (i.e., adipocyte differentiation and molecular mechanisms involved in weight homeostasis) for abnormal programming by estrogenic chemicals, and provide evidence that support the scientific hypothesis termed “the developmental origins of adult disease”. The association of environmental estrogens with obesity and diabetes expands the focus on the diseases from intervention/treatment to include prevention/avoidance of chemical modifiers especially during critical windows of development.

* The author is now retired but the work was conducted while she was employed by NIEHS/NIH.
Results from the Salmon in Pregnancy Study (SIPS): Study design and effects on maternal and infant nutritional status

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Oily fish is a rich source of n-3 long chain polyunsaturated fatty acids, vitamin D and other vitamins and anti-oxidants (e.g. Selenium). The UK government recommends that pregnant women consume 1-2 portions of oily fish per week, but the current intake for most pregnant women is lower than this. The Salmon in Pregnancy Study investigated the impact increasing oily fish intake in pregnancy where the infant expected had a higher risk of developing allergic disease (i.e. ≥1 first degree relative had allergic disease). Outcomes were maternal and infant nutrient status, infant growth, infant allergic disease markers, and manifestations at birth and 6 months.

Pregnant women (n = 123) with high risk of having atopic offspring and with low habitual intake of oily fish (≤ 2/month) were randomised at 20 weeks of pregnancy to either consuming two portions of farmed salmon a week or continuing their habitual diet until the end of their pregnancy. The women attended a clinic in the fasted state at weeks 20, 32-34, and 38 of pregnancy, at which blood samples were collected, and health and food frequency questionnaires completed. Umbilical cord blood was collected at birth. Maternal and infant blood nutrient status and immune cell phenotypes were determined. Infants were followed until 6 months of age when they were assessed for atopic outcomes.

This work was supported by the European Commission under Framework 6 as part of the AquaMax project (FOOD-CT-2006-016249-2).

Genes and nutrition: The impact of fatty acid desaturase (FADS) polymorphisms on long-chain polyunsaturated fatty acid levels

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Availability of LC-PUFAs is important in every stage of human life. Tissue concentration of LC-PUFAs is mainly dependent on dietary intake or on the intake of precursors, which are elongated and desaturated by the delta5- and delta6-desaturase. In 2006, we identified an association between genetic variants in the desaturase encoding genes (FADS1, FADS2) and the level of n-3 and n-6 fatty acids, which was replicated by various studies. The importance of FADS polymorphisms for the regulation of milk fatty acids was recently shown and we confirmed this result in a replication study. Eleven polymorphisms in the FADS cluster were genotyped and associations with fatty acid levels of maternal milk after 1.5 and 6 months of breastfeeding in 769 and 464 mothers, respectively, were calculated. We found strong associations between FADS genotypes and arachidonic acid levels (corrected p-values between 0.007 and 0.04). It is therefore likely that beside maternal nutrition, the FADS genotype determines the efficiency of a breastfed child’s supply with arachidonic acid. In addition to association studies, the identification of the functional relevant DNA variants is necessary to understand the mechanisms by which FADS polymorphisms interact with nutritional impacts. Using luciferase reporter gene assays and DNA-affinity purification, we recently identified one transcriptional regulatory variant in the FADS gene cluster (rs968567), which affects FADS2 promoter activity by allele-specific binding of the transcription factor ELK1. We will summarize current knowledge on FADS polymorphisms and show how the inclusion of genetic analyses in future studies will help to understand gene-nutrition interactions better.

Results from the Salmon in Pregnancy Study (SIPS): Effects on neonatal immune responses and infant clinical outcomes at 6 months

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Background: There is growing interest in the potential role of anti-inflammatory n-3 polyunsaturated fatty acids (n-3 PUFAs) in the prevention of allergic disease. Objective: To determine whether oily fish intervention in pregnancy modifies neonatal immune responses and early markers of atopy. Methods: Blood was collected at birth (n=101) and at 6 months of age (n=86). Neonatal PUFA levels and immunological responses (both innate and adaptive) to various stimuli were measured at birth. Total immunoglobulin (Ig) E was measured at birth and 6 months of age. Infants attended a clinic at 6 months of age for assessment of allergic sensitization (skin prick test [SPT]) and presence and severity of atopic dermatitis. Results: Oily fish consumption during pregnancy was associated with significantly lower neonatal regulatory (IL-10) cytokine responses to both LPS (p<0.05) and PHA (p<0.05). Similar trends were also seen for TNFα (pro-inflammatory) and IFNγ (Th1) protein responses, however these were not statistically significant. There were no statistically significant differences in total IgE at birth or 6 months of age. Conclusions: Oily fish intervention in pregnancy modified the pattern and magnitude of neonatal immune responses; however it did not affect early markers of atopy. Further assessment of cellular immune function and clinical follow-up of these infants will determine if there are any effects of maternal oily fish intake on postnatal immune development and expression of allergic disease. This work was supported by the European Commission under Framework 6 as part of the AquaMax project (FOOD-CT-2006-016249-2).
DHA in colostrum and fish, seafood products, fat used for cooking, n-6 fatty acid consumption during the third trimester of pregnancy in the EDEN mother-child cohort (Study of pre- and early postnatal determinants of the child’s development and health)

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Background: Colostral bioactive factors as long-chain-polysaturated-fatty-acids (LC-PUFA), docosahexaenoic (DHA) can exert regulatory functions in neonates early during the first days of life. LC-PUFA composition results from mother’s nutrition, mobilization from storage and de novo synthesis. Objective: We aimed at investigating the contribution of mother’s nutrition during pregnancy, especially through fish and seafood products, on colostrum DHA concentration. Procedure: Colostrum fatty acid composition of 383 lactating mothers aged 295years from the EDEN mother-child cohort was performed by direct transmethylation and gas chromato-graphy. Mothers usual diet during the last trimester of pregnancy was determined with a food frequency questionnaire from which were derived frequency of fish and seafood products intake (categorized in quartiles), type of fat used for cooking and n-6 intake from food. Results from dietary variables with colostrum DHA concentration was analysed by multivariate regression adjusted on maternal age, day of colostrum collection after delivery. Results: The mean (sd) frequency of fish and seafood products intake was 9 (7) per month. 19% of women always used oil for frying. The colostrum DHA concentration was 0.66% (0.26) and was positively associated with mother’s age (p<0.0001), fish and seafood intake (p<0.0001) and oil for frying (p=0.009). On the contrary, day of collec-tion (p=0.03) and intake of n-6 (p=0.03) had a negative effect on milk DHA level. Conclusion: Both increasing fish and seafood intake in pregnant mother and limiting n-6 intake are potential means to increase DHA level in colostrum. The reason for higher DHA level in older women has to be further investigated.

Results from the Salmon in Pregnancy Study (SIPS): Maternal and fetal metabolic, hormonal and inflammatory status

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Salmon is a rich source of n-3 long chain polyunsaturated fatty acids and other nutrients. The Salmon in Pregnancy Study investigated the impact of having two weeks portions of farmed salmon in pregnant women (n =123) at weeks 20, 32-34, and 38 of pregnancy Umbilical cord blood was also collected at birth. Secondary outcomes of the study were maternal and infant plasma levels of glucose and plasma lipid fractions, insulin, leptin and adiponectin, oxidative stress status (plasma lipid hydroperoxides and urinary 8-OH-deoxyguanosine), enzymatic antioxidant defense system (catalase, superoxide dismutase, glutathione reductase-GR- and glutathione peroxidase-GPOX- erythrocyte activities) and non-enzymatic antioxidant system (plasma α-tocopherol, y tocopherol-TE-, retinol, oxidised and reduced coenzyme Q10) as well as some inflammatory biomarkers (Hepatocyte Growth Factor Interleukin-6 (IL-6), IL-8, Monocyte Chemotactic Protein 1 (MCP-1), Nerve Growth Factor (NGF) and Tumor Necrosis Factor α (TNF- α) and some biomarkers of endothelial damage (e-selectin, Soluble Interleukin Adhesion Molecule 1 –sICAM-, Soluble Vascular Adhesion Molecule 1 sVCAM Matrix metalloprotease-9- MMP9- and total Plasminogen Activator Inhibitor 1 (PAI-1)). Insulin and leptin increased over gestation parallel to triacylglycerols while adiponectin decreased. HGF also increased and y TE and CoQ10 decrease, and GPOX and GR increased. sICAM, VCAM and PAI-1 increased during gestation. No major changes were observed for the analysed parameters between the intervention groups over gestation excepting that in the salmon group MMP9 and ICAM were lower. No differences were observed at birth between groups.

This work was supported by the European Commission under Framework 6 as part of the AquaMax project (FOOD-CT-2006-016249-2).

B.5: Gender effects in programming

Friday, May 7th, 16.30 – 18.05

Gender-specific differences in essential fatty acid metabolism

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Sexual hormones may influence the enzymes of the synthesis of long-chain polyunsaturated fatty acids (LC-PUFAs) and may lead to gender-specific differences in LC-PUFA status. Isotope studies with U-13C alpha-linolenic acid (C18:3n-3, ALA) found considera-
ably higher conversion rate of ALA to n-3 LC-PUFA in women [Burdge et al, Brit J Nutr 88: 411-420, 2002] than in men [Burdge et al, Brit J Nutr 88: 355-363, 2002]. In concert with these findings, significantly higher contribution of docosahexaenoic acid (C22:6n-3, DHA) to hepatic phosphatidylcholines was reported in female than in male rats [Burdge et al, Prostaglandins Leukot Essent Fatty Acids 78: 73-79, 2008], and estrogenic effects were related to enhancement of the contribution of DHA to plasma cholesteryl esters in humans [Gilley et al, Am J Clin Nutr 80: 1167-1174, 2004]. Though review of the literature generally suggests higher contribution of DHA to blood lipids in women than in men [Childs et al, Proc Nutr Soc 67:19-27, 2008], gender-specific differences were not seen in every study [e.g. Ogura et al, Lipids 45: 137-144, 2010]. Recently fatty acid composition of plasma phospholipids was reported separately for a large group of women and men (n > 3000) living at 15 regions of Europe [Saadatian Elahi et al, Am J Clin Nutr 89: 331-346, 2009]. Overall, contributions of saturated and monounsaturated fatty acids were higher, whereas those of n-6 and
n-3 LC-PUFA were lower in men than in women. However, gender explained only about 2% of the variability of plasma phospholipid DHA values. These data indicate that while gender should be taken into account in studies on LC-PUFA status, the extent of gender-specific differences remains to be elucidated.

Adiponectin concentrations during pregnancy and delivery and their relationship with anthropometrical data in newborns and children

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Aim: To investigate the relationship between maternal and cord blood plasma adiponectin and anthropometric data measured at birth and 4 years of age. Methods: Plasma adiponectin concentrations were measured in healthy mothers and their newborns participating in the NUHEAL study (n = 81) by ELISA at the 20th, 30th week of gestation, and at delivery. Results: Plasma adiponectin concentrations decreased significantly during pregnancy (20th week: 13.19 [6.24]; 30th week: 10.83 [5.18]; delivery: 10.15 [4.56]; g/ml, mean [SD], p<0.05) and were about 3-fold higher in venous cord blood (35.33 [13.89]) than in maternal blood. There were significant positive correlations between cord blood adiponectin concentrations and triceps (r=0.38, p<0.01) and subscapular (r=0.41, p<0.01) skin fold at birth. In contrast, we found significant positive correlations between chest and waist circumference of the children at the age of 4 years and maternal adiponectin concentrations at the 20th (r=0.31, p<0.05 and r=0.37, p<0.01), 30th week of gestation (r=0.38, p<0.01 and r=0.39, p<0.01) and at delivery (r=0.32, p<0.05 and r=0.42, p<0.01). Conclusion: Maternal adiponectin does not cross the placenta, so correlations between maternal plasma adiponectin concentrations in the mothers and anthropometrical data measured in their 4-years-old children might indicate that both parameters are influenced, respectively programmed, by a not yet identified maternal factor.

The work was supported by the European Communities 6th Framework Programme (EARNEST, FOOD-CT-2005-007036). va Szabo was recipient of an IRPF Young Investigator Exchange Program Fellowship.

Endocrine and growth gender differences in response to protein intake early in life.

Gruszfeld D, Socha P, Dain E, Xhonneux A, Verduci E, Koletzko B for the CHOP study group.

Background: Early high protein intake has been associated with increased growth and could programme obesity risk later in life. These effects could be mediated by protein intake stimulation on Insulin-like growth factor 1 (IGF-1) production. Aim: to analyze if males and females response differently to protein intake relating to energy intake, IGF, leptin, adiponectin, kidney size and growth at 6 months of age. Methods: multicenter European clinical trial (EU Childhood Obesity Project), about 600 healthy formula-fed infants randomly assigned to receive an infant formula with higher or lower protein content (HP and LP, respectively) for 1y. At age 6 months, blood and urine samples were collected and a kidney ultrasound was performed. Results: Females fed HP formula showed statistically significant higher levels of IGF-1 axis parameters than males (Total IGF-1 (median (IQR)): 55.15 (56.65) vs 40.95 (45.6), p<0.01). High protein intake was associated with increased IGF-1 levels independently of gender (Spearman correlation coefficient between protein intake (g/day) and Total IGF-1: r=0.243, p<0.001), but females showed a higher response. Leptin was higher in females independently of feeding group (9.0 ± 5.0 vs 7.4 ± 4.4, p<0.001). High protein intake was associated with increased urinary c-peptide/creatinine levels especially in males that showed significant differences between HP and LP groups (171.1± 138.7 vs 132.7 ± 90.9, p<0.05). Kidney volume reproduced the same gender-dependent effect (HP: 44.7± 9.6 vs LP: 40.2 ± 9.0 among males, p<0.001). Conclusion: Our findings suggest some different responses to protein supply between genders.

Maternal obesity is associated with sex-specific effects on offspring metabolism

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Maternal obesity increases the risk of cardiovascular disease in offspring. Such programmed effects may be sex-specific, although the mechanisms remain unclear. Here we investigated the hypothesis that maternal obesity causes sex-specific changes in offspring metabolism in mice. Female C57Bl/6 mice were maintained on obesogenic (58% kcal fat, 25.5% kcal carbohydrate as sucrose) or control diets for 5 weeks. Females were mated at 17 weeks, remaining on the same diets through pregnancy and lactation. Offspring of obese (DIO) and control (Con) mothers were weaned onto chow. At 3 months, offspring underwent glucose tolerance testing and were killed (n=5 females and 8 males/group); tissues were snap-frozen for analysis. At 3 months there were no differences in body weight or organ weight in male or female offspring. Female DIO offspring were hyperinsulinemic following a glucose load (AUC DIO 34.26.3 vs Con 18.92.0; p<0.05) and had increased hepatic expression of fatty acid synthase (DIO vs Con; p<0.05) and lipoprotein lipase (DIO vs Con; p=0.058). In contrast, in males, there were no differences in insulin levels (AUC DIO 128.2 58.1 vs Con 57.3 13.8; p=0.15) but hepatic expression of lipoprotein lipase, hormone sensitive lipase, PPARG, 5a- and 5-reductase (DIO vs Con; p<0.05) were increased in DIO offspring. Thus, maternal obesity is associated with programming effects in young adult mice. Crucially, these effects are sex-specific: female offspring are hyperinsulinemic, whilst males have more profound alterations in the expression of hepatic genes important in lipid and glucocorticoid metabolism in the absence of altered glucose-insulin homeostasis.
Gender-related differences in salt sensitivity of blood pressure

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Epidemiological studies have convincingly shown that drastically reducing salt intake in the community is accompanied by blood reductions that are comparable to those achieved by antihypertensive medication. Moreover, many subjects with hypertension are salt-sensitive. This implies that their blood pressure is more responsive to changes in salt intake than in subjects with normal blood pressure. Women appear to more salt-sensitive than men.

Sparse data indicate that salt-sensitivity of blood pressure is increased in subjects with low birth-weight. Experimental studies in rats have also shown that hypertensive offspring of mothers maintained on low protein diets throughout pregnancy are more salt-sensitive. However, mechanisms involved and gender-dependency are poorly studied.

Perinatal interventions aimed at persistently lowering blood pressure in genetically hypertensive rats have consistently proven to be very effective, particularly in females. Whether this is accompanied by a reduction in salt-sensitivity remains to be shown.

In sum, whether disadvantageous or advantageous developmental conditions subsequently impact on salt-sensitivity of blood pressure of adults, and whether there are gender-related differences in salt-sensitivity of blood pressure, are neglected topics that may well be of importance in public health management.

Developmental origins of health and disease: first time mothers’ views

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A convenience sample of 2070 first time mothers in five European countries [England (438), Finland (426), Germany (414), Hungary (389) and Spain (404)] self completed a questionnaire shortly after giving birth. They reported: milk feeding intentions (breast, formula, both); when they intended to introduce foods other than milk; influences on feeding intentions (family, friends, health professional, media); views on factors affecting adult health (genetics, nutrition, exercise, environmental), and the effect of a baby’s diet on life long health and disease; background socio demographic information, health and health-related behaviours. Over 80% of mothers stated that they intended to exclusively breastfeed their babies, and 23% cited a general health benefit for the baby as the reason for this decision. Although 70% stated they would not wean before six months, only 5% gave the health of the baby as a reason. Almost 90% of mothers agreed that infant feeding affected adult health, but diet as a baby was rated a very / extremely important influence on adult health by only 64%, equivalent to environmental pollution (63%). less often than diet and physical activity in childhood / adolescence (79%, 84%) and adulthood (81%, 83%). genetics / inheritance (70%), and exposure to cigarette smoke (81%), but more often than family income (24%). The most important influences on infant feeding choices were partners, ante natal midwives, staff in hospital, books and leaflets (cited by >=25% of mothers). These media may effectively promote healthy infant feeding messages. Inter and intra country differences exist.

Characterization of organic food consumers in two major pregnancy cohorts:

I Socio-demographic and lifestyle correlates of organic food consumption

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Background: It is largely unexplored to what extent preferences for organic foods in pregnancy may impact child health. Health features high among motivations for eating organic food, but it is unknown whether other lifestyle practices are in line with health recommendations. We compared socio-demographic and lifestyle characteristics of women with high and low preferences for organic foods in two large pregnancy cohorts, the Danish National Birth Cohort (DNBC) and the Norwegian Mother and Child Cohort Study (MoBa). Setting: Analyses are based on 60773 pregnant women in DNBC and 64 873 in MoBa. The questionnaires are similar in the cohorts, enabling homogeneous definitions of several variables. Questions about organic foods were phrased identically and used to define two groups in each cohort consuming organic foods nearly never (DNBC: 7155, MoBa: 33,423) or almost always (DNBC: 4154 and MoBa: 1144).

Results: Characteristics of women who almost always ate organic foods compared to those who seldom or never did so were both similar and different between the cohorts: In both cohorts the use of organic foods was associated with higher total energy intake; a preference for a vegetarian diet; engagement in physical activity; and lower BMI. In Denmark urban living, higher levels of education, higher age and occasional smoking were associated with organic foods, whereas in Norway lower age and lower levels of education were associated with organic foods. Conclusion: Associations between socio-demographic and lifestyle variables and eating organic foods are complex, and may not be reduced to one single healthy lifestyle’ orientation.
Communicating the importance of early nutrition for health in later life

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Early nutrition may have a strong influence on health and disease risk in later life. If parents are to use this knowledge to their child’s advantage, they have to be aware of this and they have to be able to act on it. Findings in the field of health psychology, however, suggest that there may be several psychological barriers which complicate effective implementation.

The work presented here investigated whether some known barriers indeed apply to the topic of communicating to parents about the influence of early nutrition on later health and disease. One quantitative and two qualitative studies among mothers and health care professionals were conducted in France, Poland and the UK. The aims were to: 1) explore whether and which barriers can be expected; 2) provide insight into why barriers can be expected and understand what can be done to address them.

The results support the idea that psychological barriers play a role in consumer understanding. For example, motivation to practice healthy behaviour may be reduced if the health effect of such behaviour is far in the future. Results indicated that mothers were less interested in effects taking place later in life compared to immediate effects. Possibilities to address this and other identified barriers were deduced from the results. In particular, it is suggested that health care professionals could play an important role in communicating the influence of early nutrition on health and disease in later life.

The availability and use of written information on infant feeding in five European countries

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This study aims to (1) investigate the importance of written information as an influence on early feeding decisions; (2) explore the characteristics of mothers who were influenced by written materials; (3) map the availability of written information for parents (leaflets and articles in the main parenting magazine) and (4) analyse the content of the leaflets and magazines articles regarding the association between feeding behaviours and health outcomes for the baby. The study was conducted in five European countries (England, Finland, Germany, Hungary and Spain). Data on sources of information on infant feeding were collected through questionnaires completed by 2071 first time mothers. Written sources of information are important to larger numbers of mothers than audio-visual approaches: one half reported they were moderately, very much or extremely influenced by leaflets or magazines.

No significant associations existed between reporting that written materials influenced infant feeding choices and mothers’ characteristics. The search (2005) revealed 127 leaflets containing an average of 4.9 statements on the health implications of breastfeeding vs formula feeding, and 2.0 on complementary feeding. The equivalent figures for magazines were 4.7 on milk feeding and 1.3 on complementary feeding. Statements on milk/complementary feeding referred mainly to protection afforded by breastfeeding against infections/foods to avoid. Written materials are potentially important means of promoting public health messages but the health implications of infant feeding choices are not consistently portrayed.

Normative Scripts in Genomics and their Social Implications

Michiel Korthals

Wageningen University, Netherlands

Like all scientific innovations, nutrigenomics develops through a constant interplay with society. Normative assumptions, embedded in the way researchers formulate strands of nutrigenomics research, affect this interplay. These assumptions may influence norms and values on food and health in our society. To discuss the possible pros and cons of a society with nutrigenomics, we need to reflect ethically on assumptions rooted in nutrigenomics research. To begin with, we analysed a set of scientific journal articles and explicated three normative assumptions embedded in the present nutrigenomics research.

First, values regarding food are exclusively explained in terms of disease prevention. Health is therefore a state preceding a sum of possible diseases. Second, it is assumed that health should be explained as an interaction between food and genes. Health is minimised to quantifiable health risks and disease prevention through food–gene interactions. The third assumption is that disease prevention by minimisation of risks is in the hands of the individual and that personal risks, revealed either through tests or belonging to a risk group, will play a large role in disease prevention. Together, these assumptions suggest that the good life (a life worth living, with the means to flourish and thrive) is equated with a healthy life. Our thesis is that these three normative assumptions of nutrigenomics may strengthen the concerns related to healthism, health anxiety, time frames and individual responsibilities for health. We reflect on these ethical issues by confronting them in a thought experiment with alternative, philosophical, views of the good life.
A link between early mismatched nutritional environment and development of components of the metabolic syndrome later in life has been shown in epidemiological and animal data. We aimed at investigating the contribution of such mismatch in the appearance of obesity, hypertension and atherosclerosis in adult male mice.

Dams were fed a control (C) or a low protein (LP) diet during gestation. Catch-up growth was induced in LP offspring by feeding dams with the control diet and by culling the litter to 4 pups against 8 in controls. At weaning, mice were fed either standard chow or an obesogenic diet (OB).

Adult LP offspring featured increased relative fat mass, hyperglycemia, hypercholesterolemia, and hyperleptinemia. Using microarray designed to study the expression of genes involved in adipose tissue differentiation/function, we demonstrated that the expression profile of several genes were dependent upon the maternal diet. Among the diverse genes showing altered expression, we could identify genes encoding several enzymes involved in lipid metabolism. Offspring submitted to early mismatched nutrition exhibited alterations in adipose tissue gene expression that increase their susceptibility to overweight when challenged after weaning with a HC diet.

Blood pressure (BP) and heart rate (HR) were assessed in conscious unrestrained wild-type mice by telemetry. We found that (1) postnatal OB diet increased significantly BP and HR in both OB-C and OB-LP offspring, (2) that maternal LP diet induced an altered diurnal rhythm a higher BP and HR and (3) higher plasma corticosterone concentration in LP offspring. Atherosclerosis plaque area was measured in aortic root sections of LDLr−/− mice treated in same conditions as wild type. Mice featured increased plaque area due to OB feeding but without influence of early mismatched nutrition.

Diet-induced obesity in pregnant rats is associated with abnormal sympathetic control of offspring cardiovascular function and hypertension. However, relative contribution of maternal weight gain versus the fat-rich diet per se is not known. Sprague-Dawley female rats were fed either a control (4% fat, n=12) or lard-enriched (24% fat, n=16) diet for a 10 days prior to mating, and throughout pregnancy and lactation. Although this short period of fat-feeding did not result in increase of maternal weight and hyperleptinemia versus controls, 9-month-old male telemetred offspring of fat-fed dams (OF) showed heightened cardiovascular reactivity to acute restraint stress (p<0.01 for ?systolic blood pressure (SBP) and ?heart rate (HR)) with a prolonged recovery time compared to the male offspring of control dams (OC). α1-adrenergic blockade led to normalisation of the response. Baseline blood pressure was similar in OF and OC but after dietary salt-loading (8% NaCl ad libitum for 1week) OF demonstrated higher night-time SBP (p<0.05) and increased LF/HF ratio of power spectral density of HR variability versus OC. The renal noradrenaline content was elevated in OF (p<0.05). Baroreflex gain and basal power spectral density components of the HR or SBP were similar in OF and OC. Fat-feeding in the absence of maternal obesity in pregnant rats leads to altered sympathetic control of cardiovascular function and hypertension in adult male offspring in response to established environmental risk-factors. These data allude to the developmental plasticity of the sympathetic nervous system both in utero and during suckling and the deleterious consequences of maternal fat-feeding in pregnancy.

Nutritional supplementation during pregnancy and offspring CVD risk: data from The Gambia


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Following-up the offspring of maternal nutritional supplementation trials provides a useful resource with which to investigate the impact of nutrition during pregnancy on offspring cardiovascular disease (CVD) risk. We conducted a cross-sectional study of offspring born during two supplementation trials in The Gambia, West Africa. One trial provided protein-energy dense food supplements to pregnant (intervention) or lactating (control) women from 20 weeks gestation until delivery and was clustered at the village level. The second was a double-blind, placebo-controlled trial of calcium (1.5g/d) supplementation, also provided from 20 weeks gestation. The second was a double-blind, placebo-controlled trial of calcium (1.5g/d) supplementation, also provided from 20 weeks gestation. The second was a double-blind, placebo-controlled trial of calcium (1.5g/d) supplementation, also provided from 20 weeks gestation.

Dietary calcium during pregnancy was similarly unrelated to CVD risk factors in the offspring. These data suggest that providing supplements to pregnant women in the second half of pregnancy may have little impact on the CVD risk of their offspring, at least in a developing country setting and at the ages studied here.
Maternal intake of fish oil during pregnancy and blood pressure in the 19 year old offspring

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Background: Studies in experimental animals and humans have suggested that changes in the peri- and early post-natal intake of n-3 fatty acids can affect CVD risk factors in adult life. This has led to the hypothesis that n-3 fatty acid supplementation in pregnancy may have a beneficial effect on blood pressure in the offspring. Specific aims: The aim of the present study was to investigate the effect of supplementation with 2.7 grams of long chain n-3 fatty acids during third trimester of uncomplicated pregnancies on blood pressure in the 19 year old offspring. Design and methods: The study was based on long term follow-up of a randomised controlled trial from 1990, in which 533 pregnant women were randomised to fish-oil (2.7g n-3 fatty acids/day; n=266), olive-oil (4g/day; n=136) or no oil (n=131). In 2009, the offspring from the randomised controlled trial were invited to a physical examination including blood pressure measurements. Intention to treat analysis was performed and a t-test was used to compare blood pressure between the fish-oil and olive-oil groups. Results: A total of 243 of the offspring were studied (fish-oil n=108, olive-oil n=72 and no oil n=63). Blood pressure did not differ between the fish-oil and olive-oil groups. The unadjusted difference was -0.48 (-3.37; 2.4) mmHg in systolic blood pressure and 1.12 (-0.60; 2.84) mmHg in diastolic blood pressure. Conclusion: We could detect no effect of fish-oil supplementation during pregnancy on offspring blood pressure in adolescence.

Timing and tempo of first year rapid growth in relation to cardiovascular and metabolic risk profile in early childhood

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BACKGROUND: Growth during infancy appears to be an important determinant of cardiovascular disease (CVD) and type 2 diabetes (DMT2) later in life. OBJECTIVES: To specify which period in the first years of life is related to determinants of CVD and DMT2 in early adulthood and to investigate the association between tempo of first-year weight gain and these determinants. METHODS: Observational study using longitudinal data collected in the Programming Factors for Growth and Metabolism (PROGRAM) study of 312 healthy participants, aged 18 to 24 years, including a relatively large sample of participants born small for gestational age. Association of determinants of CVD and DMT2 with tempo of weight gain was assessed in a subgroup of 87 participants with catch-up growth in early childhood. RESULTS: Weight gain in the first 3 months of life was inversely associated with insulin sensitivity (Beta=-0.22; P=0.008) and serum high-density cholesterol level (-0.05; P=0.005) and positively associated with waist circumference (1.44; P=0.04), acute insulin response (0.21; P=0.03), ratio of total cholesterol to high-density cholesterol (0.052; P=0.01), and level of triglycerides (0.07; P=0.04) in early adulthood. Rapid weight gain during the first 3 months of life resulted in a higher percentage of body fat, more central adiposity, and reduced insulin sensitivity in early adulthood than when slower weight gain occurred during the first year. CONCLUSION: Rapid weight gain in the first 3 months of life is associated with several determinants of cardiovascular disease and type 2 diabetes in early adulthood.

Early Diet and its impact on the metabolic syndrome - effect on adipose tissue

**Helen Budge, Sylvain P Sebert, Herman P Fainberg, Don Sharkey and Michael E Symonds**

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The metabolic syndrome is a major health challenge. As it is associated with both central obesity and a chronic inflammatory state, it may have its origins in adipose tissue dysfunction. Suboptimal maternal nutrition during critical phases of fetal development can result in adverse and permanent effects on offspring. As consequent long-term illhealth is likely to be a composite of the fetal and postnatal nutritional environments, we have explored the effects of reductions in maternal dietary intake in the critical periods of early or late pregnancy followed by accelerated weight gain in early postnatal life on the metabolic milieu of offspring. A modest reduction in maternal nutrition results in upregulation of proangiogenic DNMT-1, followed by inflammation and cellular stress in intraabdominal adipose tissue depots. This not only increases the risk of the metabolic syndrome in later life, but inflammation and cellular stress are further amplified when offspring experience a higher nutritional plane after birth. This supports the possibility that an irregular pattern of adipocyte differentiation may lead to insufficient adipose tissue capacity to store fat accrued from a postnatal obesegenic environment. Furthermore, differential effects on adipose tissue stress and inflammation are accompanied by insulin resistance and ectopic lipid deposition in the kidney and myocardium. Thus, the effects of early diet are modulated by the nutritional plane of the mother during pregnancy. The metabolic syndrome is a developmental process which can be accelerated by changes in the prevailing nutritional environment, both in fetal and early postnatal life.
Nutrition restriction in late-gestation and postnatal overfeeding change metabolic preferences in skeletal muscles of sheep
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Maternal dietary restriction during pregnancy is related to development of metabolic disorders in the offspring. In addition, postnatal exposure to overfeeding leads to metabolic adaptations. The aim of the experiment was to demonstrate if foetal programming leads to changes in catabolic preferences in skeletal muscle. Twenty twin-pregnant multiparous Shropshire ewes were divided into two groups, receiving either a NORM (semi-ad libitum) or a LOW (global feed restriction, 50% of NORM) diet during the last 6 weeks of gestation. From 3-day until 6-month of age, the twin-lambs (n=39) were assigned to each their postnatal diet: CONV (moderate hay feeding) or HCHF (high-carbohydrate, high-fat) diet. From 6-month to 24-month of age, sheep were raised on the same moderate-grass based diet. Biopsies of Biceps femoris were obtained post-mortem at either 6-month or 24-month of age. mRNA levels of genes relating to glucose and lipid metabolism were measured by qPCR. Genes were grouped into four categories: 1) glucose metabolism: INSbeta, IRS1, and GLUT4, 2) regulators of oxidation: PPARa and PPARd, 3) coordinators: PGC1a and PGC1, and 4) mitochondrial FA oxidation regulators: CPT1b, UCP2, and UCP3. Preliminary results: UCP2 were down-regulated by low treatment at both 6- and 24-month of age (P<0.05). PGC1a was down-regulated by low treatment (P<0.05), and 6-month HCHF feeding (P<0.05). CPT1b tended to be up-regulated by overfeeding at 6-month of age. Conclusions: nutritional restriction during late pregnancy has substantial influence on adult body composition and fat accumulation possibly by influencing key gene functions involved in energy, fat and glucose metabolism.

Induction of muscle thermogenesis by high-fat diet in postweaning mice: association with obesity-resistance
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Adaptation to extraterrestrial environment depends on a switch from glucose utilization to catabolism of lipids from milk. Results of Palou and colleagues suggest that the postnatal switch is controlled, at least in part, by leptin absorbed from milk trough stomach to the circulation of the neonate, since leptin is known to enhance lipid oxidation in muscle via the stimulation of AMP-activated protein kinase (AMPK). These studies also demonstrated that (i) oral administration of leptin to suckling rats could imprint a lean phenotype, and (ii) in humans, leptin milk concentrations at 1 month of lactation correlated negatively with infant BMI until 2 years of age (for review, see Sanches et al, Endocrinology, 2008). The lasting effects of leptin could reflect modulation of signalling mechanisms of energy balance in central nervous system, as well as metabolic effects in muscle and other tissues of the offsprings. Our studies (Kus et al, AJP, 2008) on inbred strains of mice differing in propensity to dietary obesity, namely the obesity-resistant A/J as compared with obesity-prone C57BL/6J (B/6J) mice, showed large differences between the strains with respect to the effect of weaning to high-fat (HF) diet on thermogenesis and skeletal muscle metabolism. Measurements at 2 weeks after weaning suggest a role of muscle nonshivering thermogenesis and lipid oxidation in the obesity-resistant phenotype of A/J mice and indicate that HF diet could induce thermogenesis in oxidative muscle, possibly via the leptin-AMPK axis. The interactions between leptin and genetic background during lactation may be critical for the observed phenotypes.

Genetic markers of adult obesity risk are associated with protection from infant failure to thrive
Ken Ong 1, Cathy Elks 1, Stephen Sharp 1, Claudia Langenberg 1, Susan Ring 1, Nicholas Timpson 2, Andrew Ness 2, George Davey Smith 1, David Dunger 1, Nicholas Wareham 1, Ruth Loos 1
1 MRC Epidemiology Unit, CAMBRIDGE, UNITED KINGDOM
2 University of Bristol, BRISTOL, UNITED KINGDOM
3 University of Cambridge, CAMBRIDGE, UNITED KINGDOM

Background There is uncertainty whether early postnatal underweight or rapid weight gain has more relevance to future obesity risk. We employed genetic variants robustly associated with adult obesity in order to explore the timing of childhood weight changes that lead to adult obesity. Methods Children from the ALSPAC birth cohort were genotyped for 10 variants robustly associated with adult BMI. Eight variants which showed individual associations with childhood BMI (in/near: FTO, MC4R, TMEM18, GNPDA2, KCTD15, NEGR1, BDNF and ETV5) were used to derive an ‘obesity-risk-allele score’ comprising the total number of risk-alleles’ (range: 2 to 15 alleles) in each child with complete genotype data (n=7,146). Repeated measurements of weight and length/height from birth to age 11 years were expressed as SD scores (SDS). Early infancy failure to thrive was defined as conditional weight gain between birth to age 6 weeks below the 5th centile. Results The obesity-risk-allele score showed little association with birth weight (regression coefficient: 0.01 SDS per allele; 95% CI: 0.00–0.02), and showed a much larger association with the rate of weight gain during early infancy (0.119 SDS/allele/year; 0.023–0.216) than during subsequent childhood (0.004 SDS/allele/year; 0.000–0.005). The obesity-risk-allele score was positively associated with early infancy length gain (0.158 SDS/allele/year; 0.032-0.284) and with reduced risk of early infancy failure to thrive (OR=0.92 per allele, 0.86–0.98). Conclusions The use of robust genetic markers in a contemporary birth cohort identified very early infancy gains in weight and length SDS as the start of the pathway to adult obesity.
The human infant accumulates a substantial amount of fat during foetal life; the guinea pig is born with similar adiposity, therefore our objective was to characterise its adipose tissue (AT) development and evaluate the effect of maternal high-fat diet on offspring’s body composition. In the first experiment, hyperplasia and hypertrophy were evaluated at 3, 10, 21 and 136 d in epididymal and retroperitoneal AT using 2H2O labelling and mass spectrometry. In the second experiment, pregnant dams received a high-fat diet (40% of calories) and adiposity of their offspring was measured by NMR at d 2, 21, 54 and 97 d. Timing of development differed between fat pads. At d 3, epididymal and retroperitoneal-AT accounted for 0.07 % and 0.78 % of body weight (BW), respectively, and at d 136 for 0.97% and 1.12% of BW. Hyperplasia (FPRcell) was enhanced in epididymal-AT early in life and decreased over time (P< 0.001), while age had no effect on retroperitoneal-AT FPRcell (P = 0.179). In both AT, fractional synthesis rate (FSR) of palmitate decreased extensively from d 3 to 10, increasing again by d 21 and declining by d 136 (P< 0.001). FSR of triglycerides gradually decreased with age (P< 0.001). Maternal high-fat diet increased adiposity of the offspring at 2 and 21 d compared to reference (P < 0.05). Adipogenesis in the guinea pig is very active during early life and is altered by maternal high-fat diet, thus, it is an adequate model to evaluate maternal nutritional interventions on AT development.

C.6: Food intolerance

Saturday, May 8th, 10.00 – 11.40

Coeliac Disease: is programming possible?

M Luisa Mearin
Leiden University Medical Center, the Netherlands. For the PreventCD study group

Coeliac disease (CD) is an autoimmune disorder that occurs in genetically predisposed individuals. CD is caused by an inflammatory T-cell response to the storage proteins in wheat, rye and barley, collectively called gluten. Ingestion of gluten by CD patients results in alterations of the small intestinal mucosa and in a variable clinical presentation: from a clear malabsorption syndrome, to anemia, osteoporosis or infertility. The treatment is adherence to a gluten-free diet. The prevalence of CD is 0.5-1%, which means that at least 2.5 million Europeans are affected. The health burden of CD is considerable, as it increases overall mortality risk, reduces quality of life and, on a societal level, has extensive negative economic consequences. Prevention of CD is strongly warranted. The Swedish epidemic on CD in the mid-1980’s and epidemiological studies suggest that infant feeding practices may have a significant impact on the risk of developing CD. PreventCD (www.preventcd.com) is a European multicenter project that studies the influence of infant feeding on the risk of developing CD, and its relation to genetic and immunological factors. The hypothesis is that it is possible to induce tolerance for gluten by exposing infants to small quantities of gluten preferably while they are still being breast fed. PreventCD encompasses: 1. a multicenter prospective double blinded randomized dietary intervention study involving infants from high risk families for CD, and, 2. a Swedish population-based CD screening study at 12-years of age in two birth cohorts that differ with respect to dietary exposures during infancy.

Physiological significance of the intake of protein-to-digest during the suckling period for the development of pancreatic digestive functions and the outcome after weaning in rats

Toshi Kinouchi 1, Daisuke Murakami 1, satomi Muraji 1, seiko Hoshi 1, tetsuo Kaneko 1, yuji Sunden 2, tomohisa Tanaka 2, takashi Umemura 3, takashi Takeuchi 3, etsumori Harada 3
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Objective: Protein matter in breast milk consists of large molecule protein for the most part. We, thus, examined the impact of large-protein-intake during the suckling period for the development of pancreatic digestive functions and the outcome after weaning, using a rat pup model. Methods: Rats were artificially reared on a standard rat formula with milk protein or a rat formula with milk protein hydrolysate (molecular weight: <3,500) from 7 to 21 days of age, and thereafter, fed a standard solid diet until 42 days of age. Pancreas weights and pancreatic digestive enzymes were measured at 14, 21, 28, and 42 days of age. At 28 days of age, we examined the pancreatic secretory ability in response to dietary protein and cholecystokinin with pancreatic duct cannulation. Results: Pancreas weights and pancreatic digestive enzymes in hydrolysate formula-fed rats were significantly lower than those in standard formula-fed rats during the suckling period and also the growing period, even 3 weeks after 2-week formula-feeding. Plasma insulin, the stimulator of amylase synthesis, was also significantly low in hydrolysate formula-fed rats, compared with standard formula-fed rats. Pancreatic enzyme secretion in response to dietary protein in rats weaned from the hydrolysate formula was significantly weaker than that in rats weaned from the standard formula. Conclusions: Our recent results suggest that the presence of large protein to digest in milk may be significant for the proper development of pancreatic digestive functions and the effects of dietary protein in infancy could remain in the later life.
Infant feeding and atopic eczema risk
Sibylle Koletzko
Dr. von Hauner Children’s Hospital, Ludwig-Maximilian University Munich, Germany

Several intervention trials evaluated infant formulae based on partially or extensively hydrolyzed proteins compared to cows’ milk formula (CMF) on their effect of atopic dermatitis. All randomized trials were performed in infants with a familiar predisposition indicated by atopic parent(s) or sibling, or elevated cord blood IgE. Some studies used additional co-interventions, like maternal dietary or environmental restrictions, or delayed introduction of complementary feeding. By far the largest trial, the German birth cohort study GINIplus, includes 5991 children. A non-interventional arm (N = 3739) followed children with or without familial predisposition. Predisposed children whose parents agreed to participate in the double-blind intervention (N = 2252) were randomly assigned at birth to one of four formulae: partially (pH-FW), or extensively hydrolysed whey (eHF-W), extensively hydrolysed casein (eHF-C) or standard CMF. Compared CMF, the eHF-C and pHF-W significantly reduced atopic eczema, while the eHF-W was ineffective. The effect developed in the 1st year of life and persisted until 6 years. Predisposed children without nutritional intervention had a 2.1 times higher risk for eczema (95% confidence interval (CI) 1.6–2.7) than children without a familial predisposition. The risk was smaller with nutritional intervention, with a HR of 1.3 (95% CI 0.9–1.9) in children fed eHF-C formula, which was not significant different to children without familiar allergy risk. It is concluded that some, but not all hydrolyzed formulae can reduce the risk for atopic eczema. However, the results cannot be generalized to infants without familiar risk for allergic diseases.

Fish oil-supplementation from 9 to 12 month of age does not affect immune markers in healthy infants
Lotte Lauritzen, Ditte L Aakjær, Hanne Frøkjaer, Camilla T Damsgaard
University of Copenhagen, FREDERIKSBERG C, DENMARK

Marine n-3 long-chain polyunsaturated fatty acids (LCPUFA) may affect immune function and immune maturation in early life. The objective of this study was to investigate if 9 months of fish oil-supplementation could modify immune function in late infancy. We performed a randomized controlled double-blinded intervention with fish oil vs. sunflower oil from 9 to 18 months of age in 106 healthy Danish infants. Before and after the intervention we measured fatty acid composition of erythrocytes (RBC), plasma IgE and C-reactive protein (CRP) as well as cytokine production in ex vivo whole-blood cultures stimulated with 20 mg/L lipopolysaccharide (LPS) or Lactobacillus paracasei for 24 h. The median intake of intervention oils did not differ between the groups (P=0.17) and was estimated to be 3.8 (interquartile range=3.2–4.2) mL/d, corresponding to 1.2 g/d n-3 LCPUFA and 2.6 g/d n-6 PUFA in the fish oil- and control-group, respectively. Fish oil-supplementation effectively raised RBC n-3 LCPUFA (P<0.001). Apart from L. paracasei-stimulated IL-10 (P<0.01), cytokine production did not significantly increase from 9 to 18 months. Preliminary analyses showed no effect of the fish oil-supplement on IgE, CRP or ex vivo IFN-?, IL-10 or IFN-?/IL-10 after LPS- or L. paracasei-stimulation. These results contradict our earlier finding of increased ex vivo IFN-? production after fish oil-supplementation from 9 to 12 months of age. This could indicate the fish oil may no longer stimulate immune maturation after 1 year of age or that sunflower oil rich in n-6 PUFA also affect the immune system early in life.

Early diet and the risk of allergy in the prospective birth cohort studies GINIplus and LISApplus.

Selected results
Stefanie Sausenthaler and Joachim Heinrich for the GINIplus and LISApplus Study Groups
Helmholtz Zentrum München, Institute of Epidemiology, Neuherberg, Germany

Objective: To give an overview about previous findings on diet in early life and the risk of allergy in the two prospective German birth cohort studies GINIplus (German Infant Nutritional Intervention and environmental and genetic influences) and LISApplus (Influences of lifestyle-related factors on the immune system and the development of allergies in childhood).

Methods: Between 1995 and 1998, 5991 infants were recruited for the non-interventional part of the GINIplus study, while 2252 infants with a hereditary risk for atopy were enrolled for a nested double blinded randomized trial assigning infants to one of 4 blinded formulas at birth. For the population-based cohort LISApplus, 3097 newborns were recruited between 1997 and 1999.

Results: Exclusive breastfeeding during the first 4 months of life showed a significant protective effect on eczema during the first 3 years of life when compared with feeding conventional cow’s milk formula. No increased risk for eczema or atopic sensitization was found when solid foods were introduced beyond the fourth months. Feeding extensively hydrolyzed casein or partially hydrolyzed whey formula significantly reduced the risk of allergic manifestations, except asthma, up to the age of 6 years in GINIplus. During pregnancy, maternal intake of margarine and vegetable oils increased while maternal fish intake decreased the risk of eczema during the first 2 years in the offspring.

Conclusion: Prevention of allergic diseases by diet may be directed towards maternal diet during pregnancy, and if breastfeeding is not possible, certain hydrolyzed formulas should be used instead of conventional cow’s milk formula.
Workshop (WS1): How to write a successful research proposal

Friday, May 7th, 08.20 – 09.25

by Dr Margaret Ashwell and Dr Elena Martin-Bautista

Dr Margaret Ashwell OBE, Ashwell Associates Ltd, Ashwell Street, Ashwell, Hertfordshire, SG7 5PZ, United Kingdom.

Dr. Elena Martin-Bautista, Junior Science Officer, European Science Foundation

The co-chairs have extensive experience in writing and evaluating grant applications at national and EU level. This interactive session will outline, and then allow participants to discuss, the ‘ten golden rules’ for writing research proposals.

1. Give the funders what they want, take all the advice you are offered,
2. What are the ‘buzz words’ in the research call?
3. Make life easy for the evaluators
4. Base everything on a good executive summary
5. Use evaluation criteria as the framework for your proposal
6. Develop a compelling argument
7. What will you do, why and how?
8. Use statistics wisely
9. Recognise the priority parts of the application form
10. Failing to prepare is preparing to fail! Ask ‘strangers’ to read critically and evaluate

Workshop (WS2): Physical activity in relation to pregnancy outcomes

Friday, May 7th, 08.20 – 09.25

Validation of measures of physical activity in pregnancy expamplied by findings from the Norwegian Mother and Child Cohort Study

Anne Lise Brantsæter, Margaretha Haugen, Helle Margrete Meltzer

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Physical activity is a complex behaviour that is difficult to assess and quantify in epidemiological studies. Self-reports of physical activity are nonetheless widely used in epidemiological studies, in spite of limited accuracy. Validation of lifestyle behaviour like physical activity is difficult and requires an objective measure as “gold standard”. Motion sensors have been shown to be a valuable objective technique for assessment of energy expenditure and physical activity both in pregnant and non-pregnant populations.

Pregnancy is a particularly difficult time for assessment of physical activity, including recreational exercise, due to the continuous physiological changes. There is no consensus regarding the effects of exercise during pregnancy and further research is needed in order to better understand how different exercise regimens influence maternal and child health. For this purpose it is important to assess the accuracy of the questions used to quantify regular exercise activity in pregnant women.

In the Norwegian Mother and Child Cohort Study (MoBa) we compared self-reported frequency of recreational exercise and corresponding metabolic equivalent (MET)-minutes with physical activity measured with the motion sensor (ActiReg®) in a validation study.

We observed significant positive associations between self-reported exercise activities and motion sensor measurements of physical activity, indicating that the questions used for exercise assessment in MoBa may be useful for ranking pregnant women according to recreational exercise level. This is important as future studies will use the same questions to explore potential associations between recreational exercise during pregnancy and a number of health outcomes of health outcomes in mother and child.

Self-reported physical activity during pregnancy in relation to BMI and blood pressure in adult offspring: Prospective study over two decades

Inge Danielsen 1, Charlotte Granström 1, Dorte Rytter 2, Bodil Hammer Bech 2, Allan Vaag 3, Sjurdur Frodi Olsen 4

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3 Steno Diabetes Center, COPENHAGEN, DENMARK

Background: Physical activity (PA) protects against metabolic syndrome and gestational diabetes mellitus increases the risk of obesity and metabolic syndrome in the offspring. We hypothesize that PA during pregnancy reduces the risk of gestational diabetes mellitus and thereby has a protective effect on metabolic syndrome in the offspring. We explored the association between PA during pregnancy and BMI and blood pressure (BP) in the 20y old offspring. Setting: PA in mid-pregnancy was assessed by questionaire in 965 women who delivered during 1988-1989. At 20y offspring completed a web-based questionaire and participated in clinical examinations.

Results: For work-related PA 173, 273, 193, and 16 women reported Mostly sedentary activity’, ‘Walking around without lifting heavy things’, ‘Walking around, lifting things and taking stairs’, and ‘Heavy physical work’, respectively. For leisure-time PA, 186, 548, 41, and 6 women reported Mostly sedentary’, ‘Light activity for at least 3 hours a week’, ‘Harder physical activity for at least 3 hours a
week', and Competitive sports several times per week', respectively. Around 20% of the women reported to participate in either one, two or three sport activities for at least one hour pr. week. Offspring BMI, systolic BP, and diastolic BP [mean(SE)] were 22.1 (0.15) kg/m2, 110 (0.65) mmHG, and 65.7 (0.42) mmHG, respectively. These outcomes did not differ statistically across various groups defined by PA measures, not even after adjusting for confounding, e.g., by maternal smoking or BMI. Conclusion: We could detect no effect of PA in pregnancy on offspring BMI or blood pressure.

Effects of maternal swimming during pregnancy on onset of body weight programming in the overfed offspring

Feng Gao, yuxi He, Lingkun Niu, Dong Dong
Hebei Normal University, SHUIJIAZHAUNG, CHINA

Objective: Overnutrition through litter size reduction programs the progeny to develop metabolic adaptations lasting into adulthood, such as hyperphagia, overweight, hyperleptinemia, hyperinsulinemia and malformation of hypothalamic nuclei. We assessed the influence of maternal swimming before or during pregnancy as a means of preventing overweight using their overfed offspring rats. Methods: Mother began swimming from 3rd day of pregnancy to delivery. On postnatal day 2(P2) pups were assigned to litter sizes of 4 and 10. Results: Maternal pregnancy swimming enhanced the opposite geotaces reflex on P14, memory ability on P21 and spontaneous motor activity on P21 in their overfed offspring. The body weight, Lee index, interval fat pads weight, serum leptin, insulin, glucose and serum total cholesterol of the overfed offspring born to maternal swimming during pregnancy (ESC) didn't significantly decrease at the weaning. On P21 the ESC rats had a significant increase in arcuate nucleus proopiormelanocortin mRNA and protein expression suggesting that this contributed to counteract overweight. However compared with the overfed offspring born to sedentary mother during pregnancy (CSC), NPYmRNA, NPY protein and LRbmRNA weren't significant differences in ESC rats. Conclusion: Pregnancy swimming may favorably influence the expression of anorexigenic POMC peptide and the spontaneous motor activity, while early overnutrition may have unfavorable effects on body weight phenotype, accumulation of internal fat and metabolic level in their offspring. Study suggests that only through the synergistic regulation among central peptides, circulation hormones and adipose tissue can pregnancy swimming prevent onset of body weighting programming of the overfed rat.

Maternal physical exercise and risk of Gestational Diabetes Mellitus, Gestational Hypertension and adverse birth outcomes: The Mother-Child cohort in Crete (RHEA study)

KATERINA SAVOULIDI 1, MARIA VASSILAKI 1, KATERINA SARRI 1, THEANO ROUMELIOTAKI 1, ANTONIS KOUTIS 1, LEDA CHATZI 1, MANOLIS KOGENINAS 2
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2 MUNICIPAL INSTITUTE OF MEDICAL RESEARCH (IMIM), BARCELONA, SPAIN

The influence of maternal physical exercise (MPE) during pregnancy on the mother and the foetus is not well clarified. We examined whether exercise before or during pregnancy are associated with gestational diabetes mellitus (GDM), gestational hypertension (GH), preterm birth and birth of neonates with foetal weight growth restriction (FWGR). We evaluated 1143 women with singleton pregnancies, recruited in the ‘sRhea’ Study (Crete, Greece, 2007-2009). Data were collected through medical records and face-to-face interviews during pregnancy. Twenty-two percent of the pregnant women (247) reported participation in any physical exercise before pregnancy and 73 women (6%) reported participation during pregnancy. The most common exercise during pregnancy was walking (71%). Compared with women who were inactive, exercising women during the index pregnancy experienced a reduction in risk of GDM (OR = 0.54, 95% CI: 0.16, 1.84) and giving birth to neonates with FWGR (OR=0.77, 95%CI: 0.27, 2.21). Women who used to exercise before pregnancy were at a lower risk of preterm birth (OR=0.81, 95%CI: 0.47, 1.38) and giving birth to a neonate with FWGR (OR=0.86, 95% CI: 0.49, 1.52) but at a higher risk of GH (OR=1.32, 95% CI: 0.45, 3.88). None of the associations reached statistical significance, as the prevalence of physical exercise among pregnant women in this study population was low. Results from this study conducted in a population of low physical activity are in agreement with the majority of studies suggesting a reduction in risk of GDM and no adverse effect for the foetus.

Workshop (WS3): Gut microbiota and programming

Saturday, May 8th, 08.50 – 09.55

The Gut Microbiota axis: The Indigenous Gut Microbiota Modulates Neurotransmission in Striatum

Sven Pettersson,
Department of Microbiology and Tumorbiology, Karolinska Institutet, 171 77 Stockholm, Sweden

Postnatal microbial colonization is an evolutionary symbiotic process modulating functions associated with immunity, nutrient intake, liver function and angiogenesis. Here we questioned whether the colonisation of the ingenious gut microbiota can affect mammalian brain development and behaviour. Using measures of exploration and anxiety like behaviours, we show that germ-free mice, devoid of gut microbiota, display a behavioural phenotype consistent with hyperactivity and reduced anxiety. This behavioural phenotype is reverted upon colonization with microbiota and is associated with changes in gene expression involving e.g. monoamine transmission and neurotrophic factors in brain regions involved in motor control and anxiety-like behaviour, as well as canonical pathways such as the cAMP second messenger system and synaptic long-term potentiation. Additional data pointing towards possible mechanisms to connect the gut-brain will be presented and discussed. Our findings suggest that postnatal colonisation of ingenious microbiota induces signalling that influences neuronal processes involved in motor and cognitive behaviour.
The interplay between both heredity and environmental factors seems to affect every stage of development from conception to early postnatal period with potential long-term effects in child and adult’s health. During pregnancy immune and metabolic functions of the foetus are dependent on the mother and the refinement of these functions seems to be initiated inside the uterus and to be responsive to the diet. The microbiota that inhabits the intestinal tract develops an array of physiological roles within the human body, influencing both metabolic and immune functions particularly during early neonatal life. At this developmental stage, the diversity of the intestinal microbiota is also highly influenced by dietary practices, which could also modify its functional roles. Shifts in the composition of the intestinal microbiota have been associated with obesity and metabolic related disorders in pregnant woman. In our studies, reduced numbers of Bifidobacterium and Bacteroides and increased numbers of Staphylococcus, Enterobacteriaceae and E. coli were detected in overweight compared to normal weight pregnant women. Moreover, some of these microbial changes were associated with serum biochemical parameters of relevance to the nutritional and health status of pregnant women and its possible effects on foetal health programming. Newborns form overweight pregnant woman also had higher birth weight than those from normal weight pregnant women, suggesting the transference of the mother’s features to their newborns. Positive correlations between the maternal intestinal E. coli numbers and infant’s birth weight and opposite correlations for Lacotobacillus numbers were found, which could be related to infant’s body weight regulation. Therefore, there seems to be associations among the mother’s intestinal microbiota, body weight and metabolic biomarkers, whose contribution to foetus health programming in uterus and to the inoculation of the newborn intestine with an aberrant or healthy microbiota after birth deserves further investigations.

Effect of non-digestible prebiotic saccharides on gut microbiota and infant’s health

**Tatiana Koch**
Manager Nutrition Science, Beneo GmbH

Breast feeding is the ‘golden standard’ for infant nourishment and nutritive functions beyond macronutrient energy supply, such as the balanced postnatal development of the immune system. Among multiple factors, establishment of the intestinal flora soon after birth plays a crucial role as stimulating factor for the development of the infant’s immune system. Oligosaccharides are believed to be an important prebiotic factor of human milk. In certain circumstances, however, a second choice infant feeding, cow’s milk based formula, is required and by the addition of appropriate amounts of non-digestible prebiotic saccharides, like inulin, oligofructose and galacto-oligosaccarides, to this formulas, it is aimed to supplement the prebiotic effect by human milk. Clinical studies in infants have shown that these prebiotic formulas significantly effect intestinal flora composition, e.g. by selectively stimulating the growth of beneficial bacteria like bifidobacteria and lactobacilli, improve stool consistency and reduce the incidence of infections and atopic dermatitis compared to formula without prebiotics. The addition of non-digestible prebiotic saccharides to cow’s milk based infant formula is a promising approach to support initial bacterial colonization and prevention of infectious and allergic diseases with impact on children’s health in later life.

A mixture of prebiotic, probiotic and LCPUFA promotes catch-up growth and prevents excessive adiposity in IUGR rats

**Euridice Castañeda-Gutiérrez, Mireille Moser, Clara García-Rodenas, Stephanie Viguet-Carrin, Katherine Macé**
Nestlé Research Centre, LAUSANNE, SWITZERLAND

We investigated the effect of supplementation with a mixture containing prebiotic (CMOS-GOS), probiotic (Lactobacillus rhamnosus), and LCPUFA (ARA and DHA) on intrauterine growth restricted (IUGR) rats. IUGR was induced by 50% maternal food restriction during last 10 d of gestation. Experimental groups (n= 24) included females and males (50:50) and were as follows: REF (non-IUGR control diet), IUGRct (IUGR control diet), and IUGRmx (IUGR mixture diet). The mixture was supplemented from d7 to d54, when a glucose tolerance test was performed and half of the animals were euthanized; afterwards all groups received a high fat diet (HFD) until d100. IUGRmx gained more weight than the others during lactation (d21), but from d22 to d54 both IUGR gained less than the REF (P < 0.05). At d54, body tended to be longer in IUGRmx than in IUGRct (P < 0.06) and not different from REF. Body fat content in IUGRmx was lower than in IUGRct (P < 0.03) and not different from REF. Basal insulin and HOMA were increased in IUGRct males compared to REF (P = 0.03), IUGRmx were not different from other groups. IUGRmx glucose AUC was not significantly different to IUGRct but greater than REF (P = 0.04). After HFD, no differences were observed due to IUGR or to early supplementation. The mixture promoted catch-up growth and normalized excessive adiposity; IUGR affected glucose homeostasis in the males but not in the females, and this was not improved by supplementation. No metabolic programming effect was observed after HFD.
Forum „Career building for new investigators“

Chair: Elena Martin-Bautista, PhD (ESF-France)
Co-Chair: Brigitte Brands, Dipl. Biol. MBE (LMU-Germany)
Hosted by Eva Szabó (UNIPECS-Hungary), Kathy Kennedy (UCLON-UK), Kirsi Laitinnen (TUCH-Finland), Sylvain Serbert (UNOTT-UK)
Speakers: Maria Rodriguez Palmero (Ordesa-Spain), Harry McArdle (University of Aberdeen-UK), Euridice Castaneda Gutierrez (Nestlé-Switzerland).

This forum dedicated to career building issues for new investigators will stress aspects of strategic career planning in the area of academics and industry. Experienced speakers from each sector will give an insight into conditions, requirements and career opportunities for new investigators enriched by an interactive panel and auditorium discussion. They will try to spotlight what is important to know before and what should be considered when strategically planning your career in either area. The questions to discuss in this forum will be the following:

1.) Young women in academia research – making it to the top?
2.) Importance and key issues of research experience abroad
3.) Career opportunities – differences between the public and the private sector
4.) Harmonization of family and work – easier in university or industry sector?
5.) Skills to develop or improve for new investigators?
6.) What are the advantages and disadvantages of working in the industry or in the academia sector for the later career of new investigators?
7.) Training opportunities: where to look for courses / summer or winter schools / scholarships?
8.) Choosing your research group: working in a big, well-known work group or joining a new work group which just starts research and establishes new methods and collaborations?
10.) How important are basic/fundamental researchers in the industry sector?

Speaker from industry/academia: Maria Rodriguez-Palmero

Today, support to mobility for young investigators in the European Union allows them to receive an excellent training. However, to design a scientific career requires drawing up a plan with specific professional objectives, choosing adequate training institutes but also taking decisions about where to develop the professional career, either at academia, research centres or industry. It is important to dedicate time to get as much information as possible about the different options, as well as to have self-knowledge to identify what are your main skills and personal values. From my point of view, industry research is always more product oriented, and necessarily involves work in multidisciplinary teams, with all the difficulties but also satisfactions that this involves. Harmonization of family and work is also an important issue that in practice is solved with commitment of father and mother, and increasing efficiency during working hours, although there is a lot to do in several other aspects (flexibility in working times, etc.). Women are specially affected by the difficulties in harmonisation between work and family, and they are still underrepresented in the research world. In Spain, very few women occupy top research positions (16.9% vs 83.1%), as revealed by a recent survey performed in the Spanish Council for Scientific Research (CSIC). Today, many initiatives are in place in order to promote access of women to top positions, such as networking, forums, etc. In conclusion, to be a young scientist today means to start a way full of challenges and opportunities!

Speaker from academia – Harry J McArdle

I am very pleased to have been asked to discuss career building in academia at this meeting. In my own case, I started in research because it never seemed like work. Even if I had won the lottery, I would still have been working in the lab. Maybe this is the best starting point. You have to be very committed. There have been a series of excellent articles in Nature discussing research careers and I recommend you go there to get information. Universities in Europe are very different and the PhD structure is also different. This is important. What about the lab? How well funded is it? Will they give you freedom or will you be in a sausage machine? What is support like? What is their success record? Then, where next? A Fellowship! If you can get your own money it is much better. Do not stay in the same lab and ideally not in the same country. Different research philosophies operate in different places. Academic careers are also very different at later stages. I am not familiar enough to comment about other European career tracks, so make sure you find out! How much teaching? What support is there for new lecturers? And of course, what about your family? In summary, a whole series of steps and decisions, but if you can deal with them a very rewarding way of spending time. Even after all these years, I still think I need to get a proper job!

Speaker from industry- Euridice Castañeda Gutiérrez (Nestlé Research Center)

Starting a career as a scientist nowadays is full of exciting decisions. Thanks to globalization there are plenty of opportunities to study and build a career anywhere in the world. As a result we also face new challenges and need improved qualifications to be competitive, which include high academic training, languages proficiency, and improved writing and communication skills. A research experience abroad can be enriching academically and personally, it provides the opportunity to learn different ways to conduct research while interacting in an intercultural environment and thus, building personal soft skills. When facing the choice
of starting to work in academia or industry, I realized there were differences but also a common ground. As a young investigator in the industry I have had the opportunity to work in multidisciplinary teams and learn about project management, regulatory affairs, communication and business, but doing research, scientific writing and working closely with the scientific community are still a major part of my job. Short term training and assistantships in the industry are great opportunities to experience this environment and evaluate if it is the right choice for you. Some of the personal skills that are valued in new collaborators are flexibility, proactive cooperation, insight and result focus attitude. Finally, whether in industry or academia I believe the most important is to enjoy and be proud of what you do, as a young investigator I see the road ahead full of opportunities and challenges and I am looking for to it!

**Industry Forum “The ways for innovation: how to foster collaboration between industry and academia”**

**Friday, May 7th 08.20 – 09.25**

**EC research to promote growth of food industry**

**Dr. Antonio Di Giulio**

*Head of Unit – Food, Health and Well-being, Directorate-General for Research, European Commission*

In Europe today, 5 out of 7 most important risk factors for premature death are diet-related. Scientific evidence from observational studies in human and experimental studies in animals shows that health problems such as hypertension, diabetes, obesity, cardiovascular disease, and bone health, and also behaviour, learning and longevity may be ‘imprinted’ at critical stage of development. Therefore, better knowledge on early nutrition programming has a huge potential for improving the health of future generations and is a long term driver for economic growth.

The new Europe 2020 Strategy puts forward priorities to promote a smart, sustainable and inclusive growth to face societal challenges. One of the key priorities of this strategy is to develop an economy based on knowledge and innovation with a target of investing 3% of GDP in Research and Development. A greater capacity for R&D as well as innovation across all sectors of the economy, both private and public, combined with increased resource efficiency will improve competitiveness of European industry in ensuring that innovative ideas can be turned into new products, foster job creation and help to address global societal challenges.

As a part of the Seventh Framework Programme, the Activity ‘Fork to farm: Food (including seafood), health and well being’ offers new research opportunities in nutrition science. This involves the development and application of nutrigenomics and systems biology in the study of the interaction between nutrition, physiological and psychological functions. The ingenuity of food technology in food formulation and production will also contribute to further advances to promote optimum health, such as personalised nutrition.

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**From the Idea to the Product**

**Ferdinand Haschke**

*Nestle Nutrition Institute, Avenue Reller 22, 1800, Vevey, Switzerland*

The innovation process in the field of paediatric nutrition starts with the project idea, recipe development and technical implementation studies. Preclinical and clinical testing under standardized conditions must prove safety and efficacy. Prior and during introduction of a new product, science based medical information to the medical community has to be provided. Health-, functional-, and nutrition claims need to be approved by regulatory authorities. How about the long-term outcome? Because no clear rules exist, industry needs to enter a dialog with scientific- and regulatory bodies. The innovation process of 2 infant formulas is described, where long-term outcome data are now available and indicate long-term safe outcome.

Improvement in protein quality allows to reduce the protein concentration in whey-based infant formula. Weight gain and BMI of infants fed those formulas correspond to breast-fed infants and are lower than in infants fed traditional formulas with higher protein concentrations. Associations between rapid weight gain in infancy and obesity later in life are confirmed by a recent meta-analysis. If infants cannot be exclusively breastfed until 4-6 months of age, feeding low-protein formulas may contribute to positive long-term health outcome with potentially important health effects for the individual.

A partially hydrolyzed whey based formula for prevention of allergic symptoms in children with hereditary risk for allergic diseases was developed more than 25 years ago. Two recent meta-analyses indicate that the risk of all allergic diseases and atopic dermatitis/eczema was significantly reduced in infants at risk when the partially hydrolyzed formula were fed. Hypoallergenic claims can be made in many countries and international nutrition committees have positively commented on the preventive effect of those formulas. Recent data from Germany indicated that weight, height, and BMI of children at 6 years of age who had been fed hypoallergenic formulas until 4-6 months of age did not differ from children who had been breastfed and served as controls.

Such long-term clinical studies cannot be done before any new product launch, because this would slow down any innovation. Therefore, clear rules have to be established by independent scientific bodies.
Challenges for industry and academia as consequences from the Health Claim Regulation: The industry perspective

Dr. Gunhild Kozianowski
Vice President Nutrition Science, Beneo GmbH

Academic research aims to explore areas beyond established science. Clinical practitioners necessarily focus largely on diagnosis and curing of diseases and thus use established markers. Main focus and challenge for nutrition scientists is an improvement of ‘health’ with the view of prevention. In order to fulfill this mandate, scientists use emerging methodologies and health markers that are not yet in clinical use, but shall reflect state-of-the-art methodology and are attributed with health relevance in scientific publications. Industry aims to implement knowledge derived from academic research into nutritional practice, i.e., foods and diets. Examples comprise healthy gut flora and pro-/ prebiotics or brain development and PUFAs. For the substantiation of such health effects, innovative food/ingredient companies invest millions of Euros for one successful product development. At certain tiers during development, non- and low-effective candidates are dropped whereas knowledge on promising candidates grows the more research is done. At a certain stage of development, when academic and industry scientists generally accept that the concept sounds credible, joint efforts are needed to allow its implementation into market products. Such an evaluation should be proportional in view of state-of-the-art expertise in the respective area as well as feasibility of human intervention studies under free living conditions. Only with academic support for claims based on credibility under considerations of state-of the art, products will be launched and made available to contribute to consumers’ health. Only under such prerequisites, companies will justify and continue to fund further research to elucidate and to eventually reach conclusive evidence after decades together with parallel verification from the use.
I-1  Pulse pressure and cardiovascular reactivity among ICSI conceived teenagers
Florence Belva1, Rebecca Painter1, Tessa Roseboom1, Jean De Schepper1, Paul Devroey1, Ingeborg Liebaers1, Maryse Bonduelle1
1UZ Brussel, BRUSSELS, BELGIUM; 2AMC, AMSTERDAM, NETHERLANDS

There is growing evidence that in-vitro fertilisation (IVF) can permanently affect cardiovascular function in the offspring. Here, we investigate whether stress response is altered in intra-cytoplasmic sperm injection (ICSI) conceived teenagers, as compared to spontaneously conceived (SC) peers. Material and Methods: Preliminary data of 118 ICSI and 162 SC children were analysed at the age of 14 years. Blood pressure and heart rate measurements were performed before and during a five minute psychological stress test (Stroop test). Pulse pressure, known as an independent cardiovascular risk factor, was calculated. All results were adjusted for auxological characteristics (sex, age, height, weight and pubertal stage). Results: Baseline mean systolic blood pressure and mean heart rate were comparable between ICSI and controls (p= 0.05). Baseline mean diastolic blood pressure was significantly lower and mean pulse pressure was significantly higher in ICSI compared to SC peers (p <0.05). During the test, mean systolic blood pressure in ICSI children decreased significantly (p<0.001) but did not change in SC children. Mean heart rate during the test increased significantly both in ICSI and in SC children (p<0.001). Mean diastolic blood pressure increased significantly and mean pulse pressure decreased significantly in ICSI children (p <0.05) but not in SC children (p >0.05). Conclusion: Preliminary data show a higher mean pulse pressure in ICSI compared to SC teenagers, at baseline. Before we can draw firm conclusions regarding an altered stress response in IVF offspring, additional measurements will be performed in the worldwide eldest cohort of ICSI children.

I-2  Are n-6 polyunsaturated fatty acids really involved in the pathogenesis of obesity?
Eszter Győrei1, Katalin Fekete1, Elvira Verduci2, Carlo Agostoni3, Tamás Decsi1
1University of Pécs, PéCS, HUNGARY; 2University of Milan, MILAN, ITALY; 3Fondazione IRCCS, Ca Granda, MILAN, ITALY

Aim: N-6 polyunsaturated fatty acids (PUFAs) have been recently related to the pathogenesis of obesity (Ailhaud, Progr Lip Res, 2006). We systematically reviewed data on n-6 PUFA status in obese as compared to normal weight subjects. Methods: The Ovid MEDLINE, Scopus and Cochrane Library CENTRAL databases were searched for trials without restriction in study design. We used formal inclusion/exclusion criteria and applied standard operation procedures for data extraction, validity assessment and meta-analysis (Lee Cooper, Am J Clin Nutr, 2009). Results: We found 5 relevant studies (1 randomised controlled trial and 4 case - control studies) comparing fatty acid composition of plasma phospholipids. Two of the studies were carried out in children (n = 93), three in adults (n = 258). No differences were seen in linoleic acid (LA) values. Gamma-linolenic acid (GLA) values were higher in one of the studies (0.26 [0.22; 0.30], % weight/weight, mean [95% CI]). In one study, significantly higher values of dihomo-gamma-linolenic acid (DGLA) was found in obese than in normal weight children (1.46 [0.95; 1.97], % weight/weight, mean [95% CI]). Both significantly higher and significantly lower contributions of arachidonic acid (AA) were reported in obese as compared to normal weight subjects; however, the pooled effect size did not show significant difference (-0.34 [-2.66; 1.98] % weight/weight, mean [95% CI]). Conclusion: Systematic review of fatty acid compositional data in obese as compared to normal weight subjects does not appear to support the concept of the pathogenic role of n-6 PUFA in obesity.

I-3 Assessing potential biomarkers of eicosapentaenoic acid status in humans: a systematic review
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University of Pécs, PéCS, HUNGARY

Aim: We systematically reviewed published data on the usefulness of different biomarkers to assess eicosapentaenoic acid (EPA) status in clinical trials. We have already reported data on docosahexaenoic acid status (Fekete et al., Am J Clin Nutr, 2009). Methods: We searched Ovid MEDLINE, EMBASE (Ovid) and Cochrane Library CENTRAL databases for intervention trials on n-3 long-chain polyunsaturated fatty acids. The minimal duration of the interventions was set at least 2 weeks; all types of supplements were considered. We used formal inclusion/exclusion criteria and applied standard operation procedures for data extraction, validity assessment and meta-analysis (Hooper et al., Am J Clin Nutr, 2009). Results: We found 36 relevant studies (27 randomised controlled trials and 9 before/after studies) reporting on 17 potential biomarkers. Based on the primary analysis of the greatest duration and the greatest supplementation dose, 4 biomarkers (total plasma, plasma phospholipid (PL), platelet and erythrocyte EPA) were found to effectively reflect changes in EPA intakes. For instance, plasma PL EPA values were reported in 16 trials (n = 759) and the weighted mean effect of supplementation was 4.07% EPA (95% CI: 2.90, 5.24). Conclusion: 1. In this systematic review, four biomarkers were found to be effectively reflect changes in EPA intakes in clinical trials carried out in humans. 2. Data generated in the present meta-analysis may be useful in answering the question which biomarker might be optimal to detect changes in EPA status in supplementation trials. Supported by the European Communities 6th Framework Programme (FP6-036196-2, EURRECA).

I-4 Maternal Food Consumption and Nutritional Status of Pregnant Women in Austria
Petra Rust, Birgit Tramnitz, Ibrahim Elmadfa
Of Nutritional Sciences, VIENNA, AUSTRIA

Nutrition is the major intruterine environmental factor that alters the fetal growth and may have influence on non communicable diseases. An essential factor is the nutritional status of women before and during pregnancy. Nutritional deficits may affect fetal growth, or may lead to abort, preterm birth, as well as abnormalities. The study investigated altogether 1580 pregnant women between 19 and 40 years in the last trimester of gestation in a representative survey on nutritional and health behaviour, within a subsample (n=...
133) of pregnant women blood samples were analyzed. Expecting women showed a suboptimal intake of folate acid, vitamin B1, B6, and D, as well as of the minerals iron, calcium, and iodine. Even though, 82% of the women took vitamin and mineral supplements, the status of vitamin D, B6, and folic acid as iron and zinc was poor. Concentrations of fatty acids in erythrocytes were not affected by dietary intake of food rich in saturated, monounsaturated or polyunsaturated fatty acids. No significant correlation was found between fish intake and n3 long chain PUFA concentrations in erythrocytes. Data show evidence that the nutritional status of pregnant women in Austria could be improved. Health education regarding the impact of water soluble vitamins, iron and zinc as well as fatty acids should be advanced to ensure an adequate nutrition during pregnancy.

**I-5 The effects of increased protein intake on kidney size and function in healthy infants: results from a randomized clinical trial**

Veronica Luque1, Joaquin Escrivano1, Ricardo Closa1, Natalia Ferré1, Marta Zaragoza1, Veit Grote2, Berthold Koletzko2, Piotr Socha3, Dariusz Gruszfeld3, Jean-Noel Van Hees4, Elena Dain5, Silvia Scaglioni6, Karl Schneider2

1Universitat Rovira i Virgili, REUS, SPAIN; 2Ludwig-Maximilians-University of Munich, MUNICH, GERMANY; 3Children’s Memorial Health Institute, WARSAW, POLAND; 4CHC St Vincent, LIEGE, BELGIUM; 5Université Libre de Bruxelles, BRUSSELS, BELGIUM; 6University of Milan, MILAN, ITALY; 7Dr von Hanaer children’s Hospital, MUNICH, GERMANY

Background: Protein intake has been associated with kidney growth and function in human observational studies. Objective: To test the hypothesis that a higher protein intake modifies kidney growth in healthy infants. Methods: This multicenter European clinical trial (EU Childhood Obesity Project) examined 601 healthy 6-month-old formula-fed infants randomly assigned within the first 8 weeks of life (median 14 days) to receive an infant formula with higher or lower protein content (HP and LP, respectively). For comparison, 204 breastfed (BF) infants were also followed. Weight and length were measured at inclusion and at 6 months. At 6 months, kidney volume was measured by ultrasonography, and blood and urine were collected. Serum-urea, serum-creatinine, urea/creatinine, urinary osmolarity, urinary creatinine and estimated creatinine clearance were determined at 6 months. Results: HP infants showed higher values than LP infants for BMI-for-age z-score (0.010.95 vs -0.221.01, p<0.01), kidney volume (cm3) (42.649.6 vs. 39.568.4), p<0.001), volume/body length (cm3/cm) (0.630.13 vs. 0.590.12, p<0.001) and volume/body surface area (cm3/m2) (111.1322.7 vs. 104.3320.87, p<0.001). BF infants did not differ from LP in any of these parameters. Boys had larger kidney volumes than girls (P<0.001). HP infants showed higher values of serum-urea and urea/creatinine ratio than LP and BF infants (P<0.05). Conclusions: High protein content of infant formula increases kidney size at 6 months of life, whereas a lower protein supply achieves a normal kidney size relative to healthy breastfed infants. The potential long-term effects of a high early protein intake on later kidney size and function remain to be elucidated.

**I-6 Habitual Nutrient Intakes during Early Pregnancy of Women Living in Ireland**

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At no point in the life cycle is nutrition more important than before and during pregnancy. Diet is a major environmental factor influencing the development of the embryo and fetus, whilst maintaining maternal health. Impaired growth and development in utero may programme the fetus for developing metabolic diseases in adulthood. The aim of the present study was to examine maternal nutrient intakes during early pregnancy. 257 healthy women were recruited from the antenatal clinic at the National Maternity Hospital, Dublin. Participants were considered for this study if they were between 10 - 18 weeks gestation, had a singleton pregnancy, with adequate English. All participants completed a 3-day food diary and recorded in as much detail as possible their food and beverage intakes. Collected data were entered into NetWISP version 3.0 (Tinuviel Software, Llanfechell, Anglesey, UK) and statistical analysis was carried out in SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Results showed that mean daily intake of certain micronutrients were insufficient and did not meet the recommended dietary allowances (RDA) for pregnancy. Mean dietary intake of folate was 271.3g (SD 111.4), vitamin D was 2.7g (SD 2.1), calcium was 877.8mg (SD 315.8), and iron was 11.1 mg (SD 3.7). Alarmingly, only 2 (0.8%) women met vitamin D recommendations, while only 8 (3.1%) women met folate recommendations. Sodium intakes were above recommended levels for the general population. These data highlight the urgent need for better public health interventions among pregnant women and consideration to fortify foods with folic acid in Ireland.

**I-7 Effects of mother’s obesity and diabetes on the folate status among pregnancy**

María Teresa Segura, Luz García-Valdés, Tania Anjos, Francisco José Torres-Espinola, Jole Martino, Miguel Marti-Romero, Rosa Maria Lopez-Turragona, Jesús Florido, Cristina Campoy

University of Granada, GRANADA, SPAIN

Several maternal conditions such as obesity and/or gestational diabetes are associated with micronutrient disorders during pregnancy. The aim of this research was to analyse the folic acid (FA) status, a vitamin that helps to prevent neural tube defects, in obese pregnant women and pregnant women with gestational diabetes (GD) in comparison with healthy pregnant women participating in Project PREOBE. Method: Venous blood collection was conducted at weeks 24 and 34 of gestation, at birth and at the 6th month postpartum. Folic acid was analysed using an automatic analyser Elecsys 2010 and the analytical E170 module (Roche, Neuilly sur Seine Cedex). Results: Throughout pregnancy, FA levels in obese women were significantly lower than those found in either healthy and GD women at week 24 (p = 0.020, p = 0.009), at week 34 (p = 0.016, p = 0.001) and at delivery (p = 0.003, p = 0.046). In contrast, there were no significant differences in FA status of the three groups at 6th month postpartum (p = 0.297). Only 25% of healthy women and 30% of women with GD were deficient in FA at the end of pregnancy while almost half of obese women (48.6%) had FA levels below 9 l/l. Conclusions: There is a decrease of the maternal FA status during pregnancy. Obesity is an important risk factor which seems to affect negatively maternal FA levels, leading to a considerable amount of obese pregnant women becoming deficient in this micronutrient at the end of pregnancy.
I-8  Effects of long-chain polyunsaturated fatty acid supplementation during pregnancy and/or lactation on neurodevelopment and visual acuity in children: a systematic review of randomized controlled trials

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Objective: To systematically evaluate the effect of PUFA supplementation of pregnant and/or breastfeeding women on the neurodevelopment and visual function of their children. Methods: We searched MEDLINE, EMBASE, the Cochrane Library, and the references in reviewed articles through December 2009 for randomized controlled trials (RCTs) comparing PUFA supplementation with placebo or no supplementation. Results: Overall, 13 RCTs were included. Among 3 RCTs that assessed the effects of LCPUFA supplementation during pregnancy on child neurodevelopment, one RCT (n=72) showed significantly better eye and hand coordination assessed with the Griffiths Mental Development Scales at 30 months of age. Another RCT (n=29) demonstrated an effect of LCPUFA supplementation during pregnancy on the visual function of the children with a higher visual acuity. Conclusions: Evidence from RCTs does not demonstrate a consistent benefit of maternal PUFA supplementation during pregnancy and/or lactation on child neurodevelopment and visual acuity.

I-9  Long-term effects of cow’s milk feeding in infancy on blood pressure and insulin resistance

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BACKGROUND: Recent studies show that the pattern of infant feeding is also associated with metabolic disturbances in later life. Results of 2001 year survey in Nizhny Novgorod city, Russia had revealed a low prevalence of exclusive breastfeeding and high incidence of whole cow’s milk feeding in infants. OBJECTIVE: To evaluate consequences of whole cow’s milk feeding in infancy on blood pressure and insulin resistance. METHODS: We studied blood pressure, glucose tolerance and insulin resistance in 79 children 4-9 years of age out of 436 children previously participated in infant feeding practice survey assessed by a pediatrician at age 1 year. Children were divided into 2 groups: 1st group of 36 children who were breastfed at least till 9 months, and the 2nd group of 43 children who had high daily volume of cow’s milk during the first year. RESULTS: Children whose diet in infancy was characterized by high consumption of whole cow’s milk showed higher systolic and diastolic blood pressure (99.58 vs 93.39 mm Hg, P<0.001; 68.23 vs 63.67 mm Hg, P=0.003, respectively). No significant differences in glucose levels, glucose tolerance indices or fasting insulin levels were observed but cow’s milk fed children demonstrated a greater upward trend in 2-hour insulin (18.5 vs 9.52 mcIU, P=0.049). CONCLUSIONS: These findings suggest that dietary patterns in infancy may have long-term effect on blood pressure and insulin level. Cow’s milk feeding in infancy may predispose children to increased blood pressure and insulin resistance at 4-9 years of age.

I-10  Gut microbiota, biochemical markers and body weight in pregnant woman

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Obesity is associated with complications during pregnancy and increased health risks in the newborn. Recent reports suggest that the nature and composition of the intestinal microbiota are related to obesity and metabolic disorders. The objective of this study was to establish possible relationships between gut microbiota, body weight, weight gain, and biochemical parameters in pregnant women. Fifty pregnant women were classified according to their body mass index (BMI) in normal weight (n=34) and overweight (n=16) groups. Gut microbiota composition was analyzed by quantitative real-time PCR in faeces and biochemical parameters in plasma at 24 weeks of pregnancy. Reduced numbers of Bifidobacterium and Bacteroides and increased numbers of Staphylococcus, Enterobacteriaceae and E. coli were detected in overweight compared to normal weight pregnant women. E. coli numbers were higher in women with excessive weight gain than in woman with normal weight gain during pregnancy, while Bifidobacterium and Akkermansia muciniphila showed an opposite trend. In the whole population, increased total bacteria and Staphylococcus numbers were related to increased plasma cholesterol levels. Increased Bacteroides numbers were related to increased HDL cholesterol and folic acid levels, and reduced triglyceride levels. Increased Bifidobacterium numbers were related to increased folic acid levels. Increased Enterobacteriaceae and E. coli numbers were related to increased ferritin and reduced transferrin, while Bifidobacterium levels showed the opposite trend. Therefore, gut microbiota composition is related to body weight, weight-gain and metabolic biomarkers during pregnancy, which might be of relevance to the management of woman and infant’s health.

I-11  High enteral energy intake is associated with an increased risk for hypoglycemia in preterm infants

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Under the nutritional regime of our department following a high caloric, protein enriched nutrition we occasionally observed asymptomatic hypoglycemia in completely enteraly fed very low birth weight (VLBW) infants. The purpose of our study was to determine the incidence of hypoglycemic episodes in this population, and to identify potential risk factors for hypoglycemia. In this single centre cohort study, VLBW infants (n = 110), born before 32 weeks of gestational age, were analyzed according to two
groups (group 1: birth weight < 1000g, n = 54; group 2: birth weight 1000 - 1499g, n = 56). A total of 4130 fasting blood glucose measurements were screened for the occurrence of hypoglycemia. The lowest value in each patient was correlated with gestational age, birth weight, nutritional intake and weight gain. Risk factors were identified by linear and multiple logistic regression analyses. In group 1, 24 of 54 infants (44.4%) experienced at least one episode of blood glucose < 45mg/dl as compared to 13 of 56 infants (23.2%) in group 2. Regression analysis identified low gestational age and high caloric intake as potential risk factors for the development of hypoglycemia. We conclude that hypoglycemic episodes in this population are asymptomatic, not sporadic and therefore, probably underestimated. Besides low gestational age at birth, high caloric nutrition appears to play an important role in the pathophysiology of hypoglycemia. Further prospective trials are required to evaluate the impact of these hypoglycemic episodes on long-term neurodevelopmental and metabolic outcome.

I-12 Energy density in infancy

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Introduction: Energy-dense foods promote excess consumption. Subjects and methods: Dietary intakes at 12, 24, 36 months were collected with a 3-days weighted food record in 83 infants participating to the multicenter European study Childhood Obesity Project (CHOP) and energy density (ED=kcal/g) was calculated as the energy from all food consumed divided by the weight of all food consumed. Only drunk water was exclude. At the same time points anthropometry was performed. Study groups included formula fed infants: 26 with lower protein content, 28 with higher protein content and 29 breast fed infants. Results: No differences in energy density according to sex was found. ED at 12m was correlated to ED at 24 and 36 months (p<0.0001) and differences in ED were found according to milk groups. Energy density at different ages and divided by milk groups is presented in the table. Data are reported as mean (95%CI), significance was calculated by Anova. Energy density at T12, T24, T36 was in all population 0.9608, 1.1144, 1.1959 (p<0.001); in lower protein formula-fed: 1.0300, 1.1948 and 1.3239 (p=0.001); in higher protein formula-fed 0.8914, 1.1073, 1.1946 (p<0.001); in breast-fed infants 0.9659, 1.0493, 1.0921 (p<0.003) respectively. Among different time points ED, according to milk groups, was significantly different (T12 p< 0.025, T24 p< 0.008, T36 p< 0.015). Conclusions: Energy density increase with age and significant differences were found according to milk group. These data suggest at 24 and 36 months a longitudinal pattern of ED with lower ED in the breast-fed group.

I-13 A prospective, randomized, double-blind crossover study comparing rhBSSL
(recombinant human Bile Salt Stimulated Lipase) added to infant formula versus placebo during one week of treatment in preterm infants born before 32 weeks of gestational age: preliminary results

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Background: The rationale for enzyme replacement therapy with rhBSSL is to restore the natural lipase activity that is absent when mothers milk is replaced with formula or human pasteurized milk. Objectives & Material: To compare the coefficient of fat absorption, growth, safety and feeding tolerance in preterm infants treated with 0.15 g/L rhBSSL or placebo. 33 infants with a mean birth weight of 1493 g and a gestational age of 32.4 weeks were randomised at a mean postnatal age of 3.3 weeks to receive one-week treatment with rhBSSL and placebo. 32 infants completed the study. Key efficacy results: A mean improvement in body weight of 3.7 g/kg/day was observed during treatment with rhBSSL (mean 18.1, SD 4.0) as compared to placebo (mean 14.3, SD 6.5) (p <0.001). Analysis of additional data is ongoing. Safety results: There were 18 TEAEs (treatment emergent adverse events) reported in 39% of the infants during rhBSSL treatment and 35 TEAEs reported in 52% of infants when receiving placebo. The most commonly reported AE in both groups was diaper dermatitis. One serious adverse event occurred during the study. The patient experienced meningitis during the placebo period and subsequently died. The investigator considered the SAE as not related to study drug. Conclusion: In this first clinical study of rhBSSL added to infant formula in preterm infants there was a significant improvement in weight gain compared to placebo after 1 week of treatment. The safety and tolerability profile of rhBSSL added to formula was similar compared to placebo.

I-14 Leptin and adiponectin in the first six months of life

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Aim: leptin and adiponectin are adipokines with important roles in energy homeostasis regulation. Recent evidences suggest that these hormones might be involved in perinatal development. The aim of our study was to evaluate the relation between serum leptin and adiponectin concentration in infants and the kind of feeding and to evaluate hormones levels in breast milk (BM). Methods: We enrolled 171 AGA healthy infants aged <6 months, without gastrointestinal disease, admitted to our Department. Serum leptin concentration has been determined by RIA test and with the same technique we evaluated leptin presence in 25 BM samples. Serum adiponectin concentration has been assessed by RIA test in 56 infants; and in 25 BM samples by ELISA. Results: Median (range) serum leptin concentration in infants was 3.85 ng/ml (0.5-36.6). Breastfed (BF) infants had statistically higher serum leptin concentration (n=95; 3.85 ng/ml; 0.5-36.6) than formula-fed (FF) infants (n=76; 2.5 ng/ml; 1.1-25.1). Median (range) serum adiponectin concentration was 135.7 ng/ml (38.5-260.0), without significant differences for adiponectin concentrations between BF (n=37; 136.8 ng/ml; 38.5-189.7) and FF (n=19; 130.3 ng/ml; 84.8-260). Median (range) leptin concentration in BM was 0.49 ng/ml (0.13-1.92). Adiponectin concentration was 10.08 ng/ml (1.92; 18.5). No statistically significant correlations were found between these hormones presence in infants serum and in breast-milk. Conclusion: our findings support the possibility that human milk components influence appetite and feeding behaviour of breastfed infants and arise the question if hormones contained in mothers’ milk could be taken in account for the beneficial effect of breast-feeding on obesity in children.
I-15  Glucose-tolerance test in pregnancy: flat response as a new entity
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BACKGROUND Oral glucose tolerance test (OGTT) is used in the screening of gestational diabetes (GD). There are different criteria to diagnose a GD case according to quantity of oral glucose load and serum glucose curve levels. The aims were to determine the incidence of glucose ‘flat response’ and to establish criteria to define it. METHODS 2544 pregnant women with a positive O’Sullivan test (glucose>140 mg/dl after oral load) were included. They underwent OGTT according to Carpenter-Coustan criteria. Glucose values were compared by two independent reviewers to define the glucose response and to determine the inter-observer agreement. RESULTS The incidence of GD was 14.7%. The reviewers found 111 cases (4.4%) of ‘flat response’. The overall inter-reviewers’ Kappa index was >0.8. In women with ‘flat response’, the average of difference between basal and 1st glucose was 5 mg/dl, 1st and 2nd -4.04 mg/dl, 2nd and 3rd -7.98 mg/dl; while in ‘non flat’ response was 68.32 mg/dl, -23.59 mg/dl and -25.73 mg/dl, respectively. The average of difference between each glucose measurement was significant according ‘flat’ or ‘non flat’. 98.19% of flat responses showed basal, 1st, 2nd and 3rd glucose =100 mg/dl. Differences between reviewers showed a Kappa index >0.94 (p<0.001). CONCLUSIONS As an unpublished data, glucose ‘flat response’ after 100 g OGTT can be defined when the 1st, 2nd and 3rd serum glucose level =100 mg/dl. This entity is a frequent problem (4.4%). These results provide us with new hypothesis and questions to investigate these cases, as well as its potential maternofetal consequences.

I-16  The effect of n-3 long-chain polyunsaturated fatty acid (LCPUFA) supplementation during pregnancy and lactation on maternal triacylglycerides (TAG)
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N-3 LCPUFA have TAG-lowering effects in humans, but this relationship has only been investigated in non-pregnant subjects. In the INFAT-study we examined the effect of n-3 LC-PUFA supplementation on maternal TAG profile during pregnancy and lactation. This was one of our secondary outcome parameters. Primarily the study was designed to investigate the impact of fatty acids in maternal nutrition on early adipose tissue development in the infant. A RCT with two parallel groups was performed (n=208). Women in the intervention group (n=104) were supplemented with 1.3g (1.0g DHA, 0.3g EPA) long-chain n-3 FA from 15th week of gestation until 16th week postpartum (59 30 vs. 69 35mg/dl; p=0.04). Conclusion: The physiological increase in TAG over the course of pregnancy was less pronounced in women supplemented with n-3 LCPUFA. The difference in the TAG profile represents a direct effect of the n-3 LCPUFA containing supplements and maintained their habitual diet. Results: Baseline TAG levels were similar in the intervention and control group (10231 vs. 11244 mg/dl; p=0.188). Over the course of pregnancy serum TAG level increased in both groups and decreased after delivery. Women in the intervention group had significantly lower serum TAG concentrations compared to control group in the 32nd week of gestation (177 63 vs. 217 64mg/dl; p<0.001), 6th week postpartum (68 31 vs. 84 34mg/dl; p=0.001), and 16th week postpartum (59 30 vs. 69 35mg/dl; p=0.04). Conclusion: The physiological increase in TAG over the course of pregnancy was less pronounced in women supplemented with n-3 LCPUFA. The difference in the TAG profile represents a direct effect of the intervention and indirectly reflects the compliance with the study protocol.

I-17  Title: The effect of maternal and fetal glucose homeostasis on birthweight.
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Aim: To examine the effect of glucose homeostasis on fetal weight. Methods: This is a prospective study of 340 healthy non-diabetic women. First trimester fasting glucose, 28 week fasting glucose, 34 week fetal growth and fetal anterior abdominal wall thickness (AAW) were recorded. At delivery cord glucose and birth weight was measured. Results: Maternal BMI correlated with maternal glucose, AAW and birthweight. Maternal weight gain in pregnancy was related to estimated fetal weight and birthweight. Maternal fasting glucose was positively correlated to cord glucose and birthweight. The incidence of macrosomia (>4.5kg) was significantly greater for fasting glucose concentrations in the highest quartile compared to the lowest quartile. (20.1% vs. 6.5%, p <0.05, first trimester; 23.3% vs. 9.4%, p <0.05, at 28 weeks). Cord blood glucose was related to estimated fetal weight, AAW, birthweight, length and head circumference. Conclusion: Glucose homeostasis is an important determinant of both maternal and fetal size. Maternal glucose and BMI appear to be the factors driving fetal glucose and fetal size. Manipulation of maternal dietary carbohydrate may have a beneficial effect on fetal glucose homeostasis and fetal growth, and is worthy of further investigation.

I-18  Effects of iron supplementation during pregnancy or in early life on the mental performance and psychomotor development of children: a systematic review of randomized controlled trials.
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Objective: To systematically evaluate the effects of iron supplementation during pregnancy and/or early life on the mental performance and psychomotor development of children. Design: MEDLINE, EMBASE, and The Cochrane Library were searched through December 2009 for randomized controlled trials (RCTs). Results: None of 5 RCTs individually showed a beneficial effect of iron supplementation during early life on the mental developmental index (MDI) of the Bayley Scales of Infant Development at different
ages throughout the first 18 mo. Meta-analysis of 3 RCTs (n=561) showed that compared with placebo, supplementation with iron had no significant effect on children’s MDI at approximately 12 mo (weighted mean difference [WMD] 1.66, 95% CI -0.14 to 3.47). Three of 5 RCTs demonstrated a beneficial effect of iron supplementation on the psychomotor development index (PDI) at some time points, while 2 did not. Meta-analysis of 3 RCTs (n=561) showed significant improvement on the PDI at approximately 12 mo in the iron-supplemented group compared with the control group (WMD 4.21, 95% CI 2.31 to 6.12). One RCT used the Griffiths scales and did find a beneficial effect in the iron-supplemented group compared to the unmodified cow’s milk group. Two RCTs showed no effect of iron supplementation on behaviour. There was no effect of iron on either the IQ or behavioral status of the children. Conclusions: Limited available evidence suggests that iron supplementation of infants may positively influence children’s psychomotor development, while it does not seem to alter their mental development or behaviour.

I-19  Correlations between fatty acid composition of erythrocytes and adiponectin concentrations in expecting mothers

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Aim: To investigate the correlation between erythrocyte fatty acid composition and plasma adiponectin concentrations in expecting women. Methods: We measured plasma adiponectin concentrations in healthy expecting mothers (n=81) by ELISA at the 20th, 30th week of gestation, and at delivery. Fatty acid composition of erythrocyte membrane phosphatidylcholine lipids was measured by gas chromatography. Results: There were significant inverse correlations between adiponectin and values of dihomo-gamma-linolenic acid (C20:3n-6) at the 30th week of gestation (r=-0.28, p<0.05) and delivery (r=-0.33, p<0.05). Dividing the mothers into two subgroups according to docosahexaenoic acid (C22:6n-3) values in the lowest and highest quartile, we found no significant correlations between adiponectin and fatty acid values in mothers with low C22:6n-3. In contrast, in the high C22:6n-3 group we found significant inverse correlations between adiponectin and C20:3n-6 values at the 20th week of gestation (r=-0.56, p<0.05) and at delivery (r=-0.74, p<0.01). Similarly, there were significant positive correlations between adiponectin and arachidonic acid (C20:4n-6) at the 30th week of gestation (r=0.52, p<0.05) and delivery (r=0.76, p<0.01) in the high C22:6n-3 group only. Conclusion: In expecting mothers adiponectin may have a stronger relation to the metabolism of n-6 than that of n-3 fatty acids. Higher availability of C22:6n-3 many straighten adiponectin’s negative association to C20:3n-6 and positive association to C20:4n-6. The work was supported by the European Communities 6th Framework Programme (EARNEST, FOOD-CT-2005-007036). va Szab was recipient of an IRPF Young Investigator Exchange Program Fellowship.

I-20  Obesity in Pregnancy: Implications for the Mother and Lifelong Health of the Child.

A Consensus Statement from The International Life Sciences Institute Europe Institute (ILSI Europe) round table workshop 16-18th September 2009.

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Obesity amongst pregnant women is becoming one of the most important women’s health issues for this decade. Obesity is associated with increased risk of almost all pregnancy complications; gestational hypertension, pre-eclampsia, gestational diabetes-mellitus, delivery of a large-for-gestational-age infant, and a higher incidence of congenital defects all occur more frequently than in women with a normal BMI. Evidence also suggests that a child of an obese mother may suffer from exposure to a sub-optimal in utero environment and that these early life adversities may extend into adulthood. In September 2009 ILSI Europe convened a workshop with multidisciplinary expertise from academia, government and industry to review health and nutrition in obese pregnant women, with focus on the longer term health implications.

I-21  Optimizing nutrition in very premature infants is possible and postnatal growth restriction may be limited

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Advances in perinatal care have resulted in improved survival and better prognosis in very low birth weight (VLBW) infants but postnatal growth restriction (PNGR) continues to be a ubiquitous problem. Studies in VLBW infants suggest an accumulation of nutritional deficit in the first 2 weeks and they are at risk of developing metabolism diseases in adulthood. A standard parenteral nutrition solution has been developed with a protocol in accordance to nutritional recommendations. Nutritional intakes and growth parameters have been analysed in 100 infants with birth weight <1250g. Twenty percent of infants were small for gestational age.
age (SGA) at birth (Husher and McLean). Analysis of nutritional intakes during first 2 weeks were in agreement with current recommendations, 40 kcal/kg/day and 2.4 g/kg/day of protein on average after admission in the NICU. PNGR has been limited to first 4 days of life and catch-up has been observed by the end of the first week in SGA infants and after 2-3 weeks in appropriate for gestational age (AGA) infants. At discharge, SGA infants only represent 23% of the population. While 9% of AGA infants developed a PNGR, 20% of SGA infants developed a catch-up at discharge. Optimizing neonatal nutrition in VLBW infants is possible immediately after admission in the NICU. The decrease in PNGR in VLBW infants in our NICU is significant comparing to previous cohort. Long term outcomes still need to be evaluated.

I-22 An increased fat droplet size rapidly establishes a fat gradient in infant nutrition
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Breast milk contains fat globules that are significantly larger than those observed in infant milk formula (IMF). Additionally, the fat content of breast milk is rising progressively during a nursing, which possibly affects appetite control (Hall, 1975). Our objective was to mimic this gradual increase in milk fat concentration observed during nursing by increasing fat droplet size in IMF. Several alterations in the production process were made to establish an IMF powder composition with an increased fat droplet size (FD-IMF) compared to standard IMF (CTR-IMF). The volume-weighted mode diameter, measured with a Mastersizer 2000, was 5.9 m and 0.5 m for FD-IMF and CTR-IMF, respectively. Fat gradient measurements were established as follows. At 10 min after reconstitution of both IMF powders to a final volume of 180 mL, the upper and lower 10 vol.% were collected. Subsequently, fat content of the collected samples was determined. In CTR-IMF, no gradient in fat concentration was observed at 10 min after reconstitution. In contrast, in FD-IMF a fat gradient was already present at 10 min after reconstitution resulting in an increased fat content in the upper compared to the lower 10 vol.% (3.21% vs 2.23%) of the IMF solution. In conclusion, increasing fat droplet size of IMF results in a fat gradient within 10 min after reconstitution, an interval well within normal feeding duration. Hall, B., Changing composition of human milk and early development of an appetite control. Lancet, 1975. 1 (7910): p. 779-81.

I-23 Analysis of nutritional intake and BMI in a prospective cohort: the NUHEAL study
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The aim of the present study is to evaluate dietary intake in children (n=149) at 4 years, born from healthy pregnant women participants in the NUHEAL Project, which were randomly assigned to 4 groups and received daily from the 20th week of pregnancy until delivery either fish oil providing 500 mg DHA+150 mg EPA, 400 g 5-MTHF, both or placebo, together with vitamins/minerals in amounts meeting the recommendations during pregnancy for European mothers. The dietary intake assessment was done using a food frequency questionnaire (FFQ) adapted for each country, Spanish food tables were used for nutrients and University of Granada data for fatty acids composition. No differences were shown in dietary intake of energy and nutrients between treatment groups. The Spanish children showed a higher Energy, Protein, Carbohydrate and total Lipids intake that those from Germany or Hungary. Saturated, monounsaturated and polyunsaturated fatty acids (PUFAs) as well as cholesterol and iron intake were higher in the Spanish children including DHA and EPA (P=0.000). The German children had the lowest mean intake of Carbohydrate and PUFA. Moreover, the BMI of Spanish children were higher (16,39) than German (15,68) and Hungarian (14,85). No statistical differences were shown between the four groups in any country. These results suggest that Spanish Andalusian children show a different pattern of dietary intake from German or Hungarian children, although they have a higher mean intake of DHA and EPA the rate of obesity and intake of cholesterol are higher than in the other European children studied.

I-24 The OBELIX project: Linking endocrine disruptors and obesity
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There is an urgent need to better understand underlying mechanisms and risk factors of obesity, such as the possible role of exposure to environmental contaminants. The European research project ‘OBesogenic Endocrine disrupting chemicals (EDCs): Linking prenatal eXposure to the development of obesity later in life’ (OBELIX) will test the hypothesis whether early exposure to EDCs may be a risk factor for obesity and related metabolic diseases later in life. OBELIX has five main objectives: 1) To assess prenatal exposure to major classes of EDCs identified as potential inducers of obesity (i.e. dioxin-like compounds, non-dioxin-like polychlorinated biphenyls, organochlorine pesticides, brominated flame retardants, phthalates and perfluorinated compounds) using mother-child cohorts from four European regions with different food contaminant exposure patterns; 2) To relate early life exposure to EDCs with clinical markers, novel biomarkers and health effect data related to obesity; 3) To perform hazard characterization of in utero exposure to EDCs for the development of obesity later in life, using a rodent model; 4) To determine mechanisms of action of obesogenic EDCs on developmental programming with in vivo and in vitro genomics and epigenetic analysis; and, 5) to perform risk assessment of prenatal exposure to obesogenic EDCs in food, by integrating maternal exposure through food, contaminant exposure and health effect data in children, and hazard data. This project has received funding from the European Community’s Seventh Framework Programme [FP7/2007-2013] under grant agreement OBELIX n 227391.
I-25 Determination of the quantity of maternal milk consumed by low birth weight babies in Morocco

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Objective: The overall objective is to determine quantity of milk consumed by infant using stable isotope technique during the first 6 months of life among children breastfed exclusively or predominantly. Methods: 30 couples of mother and baby were recruited, 20 women (28.7 ± 6.1 years) paired with infants of normal weight at birth (AGA) and 10 women (27.7 ± 6.6 years) paired with children with low birth weight (SGA). The amount of human milk consumed by the baby over a period of 14 days was assessed using the deuterium oxide 'dose-to-mother' technique. The mother was given 30g of deuterium-labelled water. Saliva samples were collected from both the mother and her baby. The technique also allows estimation of the baby’s intake of water from sources other than human milk and the mother’s body composition by FTIR. Results: The average quantity of the mother’s milk consumed by the (AGA) babies was 0.64 ± 0.23 Kg/day, 0.72 ± 0.27 Kg/day and 1.06 ± 0.36 Kg/day respectively at 1, 3 and 6 months after childbirth. However the average quantity consumed by the (SGA) babies was 0.45 ± 0.31 Kg/day, 0.66 ± 0.32 Kg/day and 1.00 ± 0.51 Kg/day respectively at 1, 3 and 6 months after childbirth. Conclusion: For both variables there is no significant difference between SGA and AGA groups.

The isotopic dilution method is an easy, non invasive and accurate technique for the determination of milk quantity consumed by the babies.

I-26 Influences in neurodevelopment of children at school age receiving antenatal glucocorticoid treatment.

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Background: Antenatal glucocorticoid (GC) therapy is used to treat women at risk of preterm delivery to enhance fetal lung maturation. There is increasing suspicion that this therapy programs mental and cardiovascular disturbances in later life. Objective: To explore the impact of antenatal GC therapy on neuropsychological development in children aged 7 to 9 years. Methods: 39 children (21 females) treated with 2x8mg betametasone (GC) 24h apart (and repeatedly if necessary) between the 25th and 34th weeks gestation and 39 controls underwent neuropsychological assessment. Controls were pair-matched for gestational age at delivery, gender, and current age. All subjects were appropriate for gestational age (delivered after 34+0 weeks gestation), without intensive care requirements, invasive procedures, or malformations. The test battery consists of testing cognitive performance (IQ - CPM) and movement performance (Movement ABC-2), attention test (CPT), parents questionnaires for ADHD symptoms (DISYPS/ADHS), socioeconomic status and child development, general psychiatric problems (CBPL), behavioural problems (SDQ) and children questionnaires for emotional irritability (PPK) and live events(ZLEL). A matched pairs analysis by mixed linear models were fitted to examine the impact of antenatal GC exposure. Results: Significant differences were observed in cognitive performance (IQ) (p=0.001), movement performance (p=0.04), ADHD symptoms (p=0.01) and behavioral problems (p = 0.004), but all within the normal range of the scales. The results have to be thoroughly explored for residual confounding which could not be eliminated by matching. Conclusion: Antenatal GC-treatment or GC-treatment related factors may cause a long-term influences on neuropsychological development, yet performances in normal range.

I-27 Dietary Intervention is Effective in Reducing the Glycaemic Index of Maternal Diets during Pregnancy

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Infant birthweight has increased over the past 30 years in Ireland, implying that environmental factors may be responsible for this increase. It has been suggested that consuming a low-glycaemic index (GI) diet during pregnancy may reduce the risk of macrosomia by regulating delivery of glucose to the foetus. The aim of this study was to investigate the impact of dietary intervention on the mean GI of maternal diets. 230 healthy secundigravid women were included in the analysis. 100 participants were randomised to receive low GI dietary advice and 130 received no dietary intervention. All participants completed 3 day food diaries each trimester. Collected data were entered into NetWISP version 3.0 (Tinuviel Software, UK). New food codes were created where necessary and GI values were added using the most up-to-date GI data from UK and international sources. Statistical analysis was carried out using SPSS version 14.0 and differences in mean dietary GI between the groups considered significant at P < 0.05. At baseline there was no significant difference in dietary GI between intervention and control groups respectively (50.9 vs. 52.0, P = 0.212). Following dietary intervention, mean GI was significantly lower among the intervention group during the 2nd trimester (50.4 vs. 52.2, P = 0.043) and 3rd trimester (50.6 vs. 52.3, P = 0.030). Results indicate that dietary advice was effective in reducing the mean GI of pregnant women. This finding highlights the value of dietary advice, and is an important consideration in relation to future research into associations between diet and pregnancy outcomes.

I-28 The effect of smoking cigarettes on antioxidative properties of human milk

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Background: Smoking is very common among lactating women. Antioxidative properties of human milk can be decreased by reactive oxygen species present in cigarette smoke. The influence of oxidative stress in children breastfed by smoking mothers is unrecognized. Objective: To estimate antioxidative - prooxidative balance disorders in human milk due to smoking cigarettes. Methods: A prospective cohort study - the group includes 32 smoking mothers, the reference group 29 non-smoking mothers. Inclusion criteria: natural delivery; breastfeeding; smoking determined by direct question and cotinine in urine levels. Exclusion criteria: passive smoking; chronic, acute, pregnancy related diseases; pharmacological treatment. Reference group met all criteria, except from smoking. Isoprostanes and Total Antioxidant Status (TAS) of human milk was estimated in 3rd and 30th day post partum. Results: TAS in colostrums was higher in non-smoking than smoking mothers (5.1 vs. 4.07 umol/l). Intensive smoking decreases TAS in milk. TAS
(4.07 vs 5.12 umol/I) and isoprostanes concentration (174 vs 261pg/ml) were lower in colostrums than in the mature milk of smoking mothers. The higher concentration of isoprostanes were detected in urine of smoking mothers (6.6 vs 4.3 ng/ml). TAS in milk was inversely correlated with oxidative stress in smoking mothers. Conclusions: Maternal smoking during pregnancy and lactation effects in reduction of antioxidative status in colostrums. TAS in milk is related to number of cigarettes smoked. Free radicals mediated damage to elements of milk augmented in smoking women in course of lactation. Oxidative stress in women is correlated with antioxidative disorders in milk.

I-29 Correlation of plasma n-3 polyunsaturated fatty acid with 24-hr dietary recall of fish intake in pregnant women in Taiwan

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Requirement of long chain n-3 polyunsaturated fatty acids (LCPUFA) increased during pregnancy due to accretion of maternal, placental, and fetal tissue. Maternal LCPUFA status is essential for maintaining an adequate LCPUFA placental supply to fetus for optimal development. In order to develop dietary monitoring method for the LCPUFA status during pregnancy, we investigated the correlation between dietary fish product intake and plasma LCPUFA concentrations. Pregnant women with fish intake > 60 g/day and no fish intake were selected from a pregnancy nutrition survey in Taiwan. The phospholipid fatty acid profiles of their plasma samples were analyzed using gas chromatography. The percentages of saturated fatty acid, monounsaturated fatty acid and polyunsaturated fatty acid in plasma total fatty acid were 36.04%, 22.08%, 41.88% in high intake women, and 41.14%, 20.98%, 37.88% in no intake women. The percentages of n-6, n-3, linoleic acid, arachidonic acid, EPA and DHA in plasma total fatty acids were 39.183.50%, 2.700.71%, 32.883.77%, 4.771.29%, 0.410.21%, 1.940.41% in high intake women, and 36.744.11%, 1.140.48%, 31.783.55%, 3.790.87%, 0.050.17%, 1.050.33% in no intake women. The arachidonic acid, EPA and DHA concentration in weight percentage was significant higher in high fish intake women than in no intake women. The low plasma LCPUFA concentration in Taiwanese pregnant women is a concern for pregnancy health. The 24-hr dietary recall provides an estimation of fish eating habit.

I-30 Elemental formula diet in autistic children

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Background: Autism is a complexed neurodevelopmental-neurobiological disorder of behaviour, which is characterized from loss in three domains: social behaviour, status of contact-speech, interests. Also, autistic children have a strong hyperactivity status and many nutritional problems. Aim: The investigation of the correlation of the autistic children’s hyperactivity status with major nutritional changes using elemental diet and testing these children for food allergies using Rast/Cap IgE tests. Patients and methods: A total number of 59 children aged 2.5 to 8 years were checked. All of them were diagnosed with pervasive developmental disorder. From the 58 children, 19 were found having positive Cap IgE tests for cow milk allergy(class 1-3) and 4 of the 19 children had multinutritional allergy. Further, the 19 children group was randomly divided in two subgroups, 9 of the children started elemental milk(containing free aminoacids-Neocate) diet(group A) and the rest 10 children continued their previous diet(group B).The other 39 children group was also randomly divided in two subgroups, 19 children started elemental milk(containing free aminoacids-Neocate) diet(group C) and the rest 20 children continued their previous diet(group D). Results: After 4 months of observation, statistical significant differences (p<0.001) were found in hyperactivity status(measured using proper questionnaire model) between groups A and B, also between groups C and D. Conclusion: Children suffering from pervasive developmental disorder have increased hyperactivity status but it seems that elemental diet has much to offer in order to lower hyperactivity levels, not only in autistic children with proven food allergy, but in all of them.

I-31 Serum phospholipid n-3 fatty acids during pregnancy - can we interact with dietary counselling?

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Background: Maternal n-3 fatty acids (FA) are important immune regulators with likely health benefits for both mother and child. The aim here was to explore whether serum phospholipid FA composition of pregnant women may be modified by dietary counselling. Methods: At the first trimester of pregnancy women were randomized to receive counselling (n=44) or as controls (n=44). The counselling aimed to modify dietary intake according to current recommendations focusing on the amount and type of fat. Subjects also received conventional food products to be used at home e.g. spreads and salad dressing. Results: Dietary intervention was reflected as a higher proportion of sum of FA and phospholipids were analysed by gas chromatography at the 1st (baseline) and the 3rd trimester of pregnancy. All women participating in the study also attended municipal well-women clinics. The accomplished changes in maternal serum FAs may induce health benefits in the off-spring group, 4.6% (95% CI 4.3-4.9), p=0.033. Conclusion: Serum phospholipid n-3 FAs may be increased by dietary counselling supported via programming effect.

I-32 Establishing a healthy growth trajectory in formula-fed infants: the BabyMilk trial

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Background: In 2004, based on new data on energy expenditure, the World Health Organisation lowered the recommended energy requirements for infants by 15 to 20%. Current formula-feeding instructions in the UK correspond to the earlier 1985 WHO
recommendations and this may contribute to the faster weight gain in formula-fed compared to breastfed infants. BabyMilk is an explanatory randomised controlled trial to evaluate the efficacy and acceptability of a theory-based, multi-component behavioural intervention to lower formula-milk intake (based on 2004 WHO recommendations) and prevent excessive infancy weight gain.

Intervention: To develop and optimize the intervention and evaluation tools, we undertook two systematic reviews and performed qualitative studies with mothers and a range of healthcare professionals. The intervention is based on Social Cognitive theory and includes a motivational component, a component to help translate motivations into actions, and support for mothers to cope with difficult infant behaviour. 700 formula-fed infants will be randomized to receive standard advice or the intervention, which involves three face-to-face contacts and two telephone contacts during the first six months of life in addition to theory-based leaflets and materials. Outcomes: The primary outcome will be weight gain from birth to 1 year, conditional on birthweight. Secondary outcomes include infant anthropometry, milk and dietary intakes, sleeping and other behaviours. Process measures such as psychological mediators of the intervention will also be measured. Conclusion: The BabyMilk trial will enhance understanding of the factors related to excessive infant feeding and weight gain and will inform future strategies for obesity prevention.

I-33 Prebiotic oligosaccharides in the Prevention of Atopic disease
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Introduction: Emerging evidence suggests a link between the intestinal microbiota in infants and the development of atopic diseases. This study was designed to elucidate the role of the intestinal microbiota and prebiotics in relation to atopic dermatitis and asthma. Study design: 200 infants at high risk for atopy (parental history of atopy) were included from 2004 until 2006. Mothers were encouraged to breastfeed as long as possible. A nutritional intervention was performed in a double-blind, randomized, parallel manner from start of formula feeding until 1 year of age with a hypo-allergenic start formula with or without a mixture of neutral (scGOS/leGOS) and acidic oligosaccharides (pAOS). Faecal samples were collected at the age of 3 weeks, 6 months and 1 year. Intermediate results: To date we can only provide preliminary data, since the study is still completely blinded and the investigations at the age of 4 years are to be completed. At the age of 1 year sensitization to food allergens was seen in 11%, sensitization to the inhalant allergen house dust mite only in 2% and to both in 1% of the children (114 tested). At the age of 4 years 24% were tested positive to inhalant allergens, only 4% to food allergens and 3% of the children to both (72 tested so far). Perspectives: The unblinding, the analysis of the faecal samples and the follow-up until the age of 6 years will provide an answer to the question: ‘Can prebiotics reduce the incidence of atopic diseases?’

I-34 In vitro and clinical evaluation of new rice protein hydrolysates for the treatment of cow’s milk allergy in infants
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Hydrolysed rice protein formulas have been used as alternatives to hydrolysed cow’s milk formulas or soy protein formulas in the treatment of allergy to cow’s milk proteins in infants. The objective of the present study was to characterise and to evaluate different rice hydrolysates using in vitro tests, and secondly to evaluate clinical tolerance and efficacy of a hydrolysed rice based infant formula (Hz-RPF) in infants with diagnosed cow’s milk allergy. Methods: The IgE reactivity of four different rice hydrolysates was evaluated using sera of patients with clinically demonstrated allergy to cow’s milk proteins that contains at least 20 KU/L of specific IgE antibodies towards milk proteins, measured using FEIA-CAP System. IgE binding was measured using an indirect ELISA coupled to a signal amplification system. Clinical efficacy of the formula was measured by a prospective, randomized study in 92 infants diagnosed with IgE mediated cow’s milk allergy, in comparison with extensively hydrolysed protein formula (Hz-CMPF). The duration of the study was 24 months. Clinical tolerance to the formulas was not different between the groups, and infant growth was also similar. The number of infants who did not become tolerant to cow’s milk protein during the study was not statistically different between the 2 groups. Measurement of IgE levels of infants allergic to cow’s milk protein during the study showed no significant differences between the 2 formula groups. The new hydrolysed rice protein formula is a safe alternative for the treatment of cow’s milk allergy in infants.

I-35 The effects on daily consumption (in volume, protein intakes and growth) of the Novalac Satiété in voracious infants.
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A rapid weight gain during the 4 first months of life might be correlated to an increased overweight risk at 7 year-old. Aim of the Study: This study is to assess, in voracious infants, the evolution of weight gain, Zscore daily intakes in volume, DRI percentage, protein intakes versus standard formulae.
I-36  Marine n-3 fatty acid status in infants and their mothers
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NIFES, BERGEN, NORWAY

Dietary n-3 fatty acids are important modulators of inflammation. The enzyme indoleamine 2,3-dioxygenase (IDO) is induced by interferon-γ secreted by activated T cells, and leads to tryptophan (Try) degradation to kynurenine (Kyn). An increased Kyn/Try ratio is associated with systemic inflammation. In the present study maternal and infant dietary information were collected and fatty acid composition of red blood cells was analysed in mothers and infants at 6 weeks (N=38) and 4 months (N=55, N=51, respectively) and related to maternal and infant Kyn/Try ratio. The fatty acid composition of the mothers was compared to blood samples of healthy, fertile, nonpregnant women (N=63). In general, the mothers had a lower total n-3 fatty acids status compared to the reference women both at 6 weeks and 4 months postpartum. At 6 weeks postpartum, the fatty acid profile of the child reflected the maternal profile regardless of breast feeding habits. Daily infant intake of cod liver oil was associated with a lower Kyn/Try ratio in infants at 6 weeks and 4 months.

I-37  Changed HLA axis and autonomic stress reactivity of children at school age as long-term effect of antenatal glucocorticoid treatment.

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Objective: To explore the impact of antenatal glucocorticoid for lung maturation on autonomic nervous system (ANS) stress reactivity in children aged 7 to 9 years. Methods: 39 children (21 females) treated with 2x8mg betametasone (GC) 24h apart between the 25th and 34th weeks gestation and 39 controls underwent the Trier Social Stress Test (TSST-C). Controls were pair-matched for gestational age at delivery, gender and current age. All subjects were appropriate for gestational age (delivered after 34+0 weeks gestation), without intensive care requirements, invasive procedures, or malformations. salivary cortisol levels were measured during TSST-C. Standard indices of heart rate variability (HRV) were derived from the electrocardiogram as outcome measures: mHR (mean heart rate), SDNN (overall variability), RMSSD, HF (both related to vagal activity), LF (related to vagal and sympathetic activity), LF/HF (sympatho-vagal balance), AIF (autonomic information flow). A matched pairs analysis by mixed linear models were used. Results: The cortisol stress response was blunted in the GC group (p=0,015). Adjusted for baseline activity TSST-C induced a attenuated increase in meanHR, LF/HF and AIF and a attenuated decrease in SDNN, RMSSSR and HF in the GC group compared to controls. This suggests a blunted stress response of all parts of ANS in GC group. The results have to be thoroughly explored for residual confounding which could not be eliminated by matching. Conclusion: The reduced stress response of the hormonal and autonomic nervous system in children may have been programmed by antenatal GC administration.

I-38  Effect of Dietary Iron Deficiency Anemia on Pregnancy Outcome
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To evaluate the effect of dietary iron deficiency anemia on pregnancy outcome and duration of gestation, female albino rats of Wistar strain, with similar body weight (180-200g) were fed on iron deficient diets (30, 15, 7, 2mgFe/kg of diet) and iron sufficient diet (50 mgFe/kg of diet) for about one month. ACTH Hormone assay was performed. The gestation period, number of neonates and weight of neonates were compared with that of controls. No significant difference was observed in the number and survival of the fetuses, with decrease in the dietary iron contents of the maternal diets. A significant (p<0.001) reduction in the gestation period was observed in the iron deficient anemic mothers. The weights of the neonates of the iron deficient females were found decreased significantly (p<0.001). Two-way analysis of variance showed a very significant (p<0.001) rise in the level of ACTH when analyzed with two grouping factors (iron status and stages). With the decrease in the maternal dietary iron contents, high ACTH was observed which in turn probably caused the stimulation of corticotropin releasing hormones in the fetuses and resulted into stress. The blocking effect of progesterone diminishes and leads to the preterm delivery. The low neonatal weight was due to insufficient supply of nutrients to the developing fetuses.

I-39  Translation of dietary odorants into human milk - molecular and physiological considerations
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Objectives. A series of behavioral and sensory studies indicate that dietary food aromas from maternal diet might translate into human milk. In a recent study applying concentrated encapsulated aroma models for maternal supplementation, odorant passage into human milk has also been demonstrated on a molecular basis. Nevertheless, data on food aromas relevant in everyday maternal diet are not at hand. Therefore, the aim of the presentation is to highlight the relevance of aroma transfer into human milk based on molecular and physiological considerations. Methods. Odor-active substances were characterized in exemplary foods by means of gas chromatography-olfactometry and identified on the basis of their mass spectral and chromatographic characteristics. The target substances were quantified by application of stable isotope dilution assays, both in the original food materials, as well as in human milk obtained from mothers after consumption of these foods, in comparison to a control group without ingestion of these foods. Results. Balancing of the total ingestion in relation to the amounts of odorants detected in the milk samples showed that neither fish oil aroma nor fenel-anise-carvone tea aroma translated into the human milk. The data will be discussed based on quantitative, resorptive, metabolic, and general pharmacokinetic considerations. Conclusions. Investigations of our group show that aroma translation into human milk from maternal diet does not necessarily occur but depends on the molecular composition of these aromas, as well as the respective concentrations of the odor-active substances. Funding. Financed by the German Federal Ministry of Education and Research (BMBF).
I-40 Effects of Different Feeding Types on the Physical Growth of Children from 0-1 year

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Objective: To find out the effects of different feeding types on the physical growth of infants aged 0-1 years. Methods: The infants who visited the child health clinics at regular intervals were classified as exclusively breast-feeding group, bottle-feeding group, and mixed feeding group according to the feeding types before 4 months. The growth indices were measured and the WHO BMI standards were used to assess overweight and obesity. Results: As for male infants, the height and weight of breast-feeding group were the biggest except the first month, and the differences are statistically significant from 3-12 months (P<0.05); The weight of bottle-feeding group is the biggest except the first month, and the differences are statistically significant from 3-12 months (P<0.05). Before 3 months, the morbidity of overweight of breast-feeding group is the highest. From 4 months old and later on, bottle-feeding group has the highest incidence of overweight (P<0.05). The morbidity of obesity of breast-feeding group is the highest one except 2 months old (P<0.05). Conclusion: The incidence of overweight and obesity of bottle-feeding group is the highest one among the three groups. Breast-feeding seems to have potential effect to protect infants from obesity.

I-41 Dietary intake and nutritional status of children borne with a low birth weight

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Low birth weight is not only the one of the most important determinants of mortality, morbidity and disability in infancy and childhood but also has a long-term impact on health outcomes in adult life. Inappropriate fast 'catch-up' growth after birth in babies born small for gestational age plays key role as primary predisposing factor in the etiology of diabetes mellitus type 2 and metabolic syndrome. That might be modified by early childhood nutrition, including breastfeeding. The aim of the study was to estimate the nutritional and nutritional status of children with low birth weight. The study was conducted in 21 children aged 7 to 15 years (11 girls, 10 boys) with the average birth weight of 2127.469.9g. Nutrient intake was evaluated on the basis of collected 3-day dietary records provided by parents. Basic anthropometric measurements (weight, height) were conducted and nutritional status was assigned based on Cole factor. Nutritional status for the age was adequate in almost 43% but 10% of children were undernourished. The nutritional data showed insufficient level of energy and carbohydrates and excess of fat and saturated fatty acids comparing to dietary guidelines. Moreover the amount of sweets and sugars was too high. The intake of vitamins: B1, PP, C and minerals: calcium and iron was low. Observed nutritional habits might increase the risk of obesity, cardiovascular diseases and diabetes type 2 in adult life in children born with a low weight. So regular dietitian support leading to changing nutrition manner is strongly recommended.

I-42 Visceral adiposity cut-off values to indicate risk factor to develop the NAFLD in Brazilian obese adolescents

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Background: Visceral adiposity distribution also appears to influence metabolic complications, being a risk factor for the development of non-alcoholic fatty liver disease (NAFLD). Aims: To determine a visceral adiposity cut-off to indicate risk factor to develop the NAFLD in Brazilian obese adolescents. Methods: 151 Brazilian post-pubertal obese adolescents (BMI > 95th of the CDC reference charts) were enrolled. Visceral, subcutaneous and NAFLD fat were analyzed by ultrasound. Visceral adiposity of obese adolescents was distributed in cut-off values using a ROC curve analysis. Results: A visceral adiposity value of 3.78 cm in Brazilian obese adolescents was the optimal cut-off values to indicate risk factor to develop the NAFLD using a ROC analysis. Indeed, it was observed, a higher prevalence of NAFLD in the Brazilian obese adolescents (86.0%) that has a value of visceral adiposity more than 3.78cm. Conclusion: Brazilian obese adolescents have a higher risk to develop NAFLD confirmed by visceral adiposity cut-off values. These findings suggest the importance to identify as early as possible the visceral adiposity cut-off points to determine NAFLD prevalence in paediatric population, in view to support a best clinical practice.

I-43 Noninvasive Method for blood glucose level estimation by Saliva

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AIMS: Diagnostic devices are available in the market to measure the blood glucose level. However in all available products blood is taken as diagnostic body fluid. So necessarity arises to find some non-invasive diagnostic mean to measure body glucose level frequently without any discomfort to the patient. Hence, the present study aimed at estimation of blood and saliva glucose level in diabetic and non diabetic subjects. METHODS: Twenty diabetic and twenty non diabetic subjects were randomly selected for this study. A detailed history of each patient was obtained regarding the age, sex, duration of diabetes, associated risk factors, family history and any associated illness. The quantitative estimation of the blood and saliva glucose level were performed by glucose oxidase method, using enzymatic kits (GOD-DAP). RESULTS: A correlation was observed between fasting saliva glucose level (SGL) and fasting blood glucose level (BGL) of diabetic as well as non diabetic subjects. The correlation coefficient of non diabetic and diabetic subjects were +0.84 and +0.34 respectively. These values of correlation coefficient proved the correlation of fasting saliva glucose and fasting blood glucose values statistically. CONCLUSION: Values observed regarding blood and saliva glucose level were found distinctly difference between normal subjects and diabetic subjects suggesting that monitoring of saliva glucose level can be used as an index of diabetes mellitus. KEY WORDS - Noninvasive, saliva glucose, blood glucose and diabetic mellitus.
I-44 Long-term evidences of combined exercise on metabolic syndrome and inflammatory state in obese adolescents

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Metabolic Syndrome is an emerging clinical problem among patients of all ages, and different kind of interventions that emphasize healthy eating and regular exercise are crucial to control this disease. PURPOSE: to compare the effect of aerobic and concurrent exercise effects on metabolic profile in obese adolescents with Metabolic Syndrome submitted to a long-term interdisciplinary intervention. METHODS: 32 adolescents aged 15-19 y., with BMI > P95 and with Metabolic Syndrome diagnosed by IDF (2005) criteria. They were submitted to long-term multidisciplinary intervention (nutrition, psychology, exercise and clinical support) after randomized to aerobic (n=11) or concurrent training (n=21). Blood samples were collected to analyze glycaemia, HOMA-IR, lipid profile, adiponectin. RESULTS: both group presented a significant reduction in the body mass, BMI, fat mass and visceral fat. However, only the concurrent exercise group improve significantly lean mass percentage, waist circumference, glycaemia, insulinemia, HOMA-IR, total cholesterol, LDL, and adiponectin. CONCLUSION: Important clinical parameters presented more altered in obese patients with Metabolic Syndrome and the concurrent exercise in a long-term multidisciplinary obesity intervention was more effective than aerobic training to improve the metabolic profile and inflammatory state commonly associated with Metabolic Syndrome in the paediatric population, emphasis the potential therapeutic implications.

I-45 Prognostic performance of routine biochemical markers for fatal protein-energy malnutrition

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Objective: The objective was to examine the diagnostic performance of routine laboratory test as a biochemical risk marker of mortality in malnourished children at admission to the hospital. Design and methods: 93 patients with PEM were examined aged from 6-60 mos. According to the clinical evolution during hospitalization patients were divided into two groups: Nosurvivors: 13 infants (15.66%) who died during hospitalization; the mean age was 11.60 months. Survivors: 70 infants (84.33%). 10 children were excluded from the study. Routine biochemical markers from 70 children with PEM, who survived were compared with those who died (13 children) during nutritional rehabilitation at the hospital. Receiver-operating characteristics curve analysis was done to determine the usefulness of the assay. Results: dead patients showed significantly lower circulating Potassium and Sodium levels. Receiver-operating characteristics curve analysis showed superior performance (e.g., sensitivity, specificity) of Potassium as a diagnostic marker of risk of death as compared against other biochemical markers (Haemoglobin, Hematicrit, Glycaemia, Urea, Triglyceride, Cholesterol, Albumin, Immunoglobulin A and CRP). Conclusions: Potassium and Sodium levels may be a promising biochemical risk marker of death. Key words: Malnourished children, Performance, risk of death and biochemical markers.

I-46 Improved isoflavone levels in menopausal hypothyroid subjects

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Introduction: Menopausal situation causes a lot of physiological and hormonal changes in woman's life. The changes are experienced at different stages of life (35-55 yrs). During this period there is a shift in thyroid functioning status and hypothyroidism is precipitated. Phytoestrogen rich foods play a key role to bridge the gap and its consumption is found to improve the hormonal imbalance. Objective: To assess the impact of consumption of Fenugreek and Sesame seeds in bringing improvement in hormonal functioning and Iodine nutrition. Materials and Methods: 50 healthy menopausal subjects (35-50 yrs) were enrolled for the study whose blood and urine samples were collected for assessing the isoflavone, FSH and urinary iodine concentration (to assess the levels of iodine deficiency). Results and Discussions: FSH assessment revealed, 50% of the population had deranged hormone levels. The subjects had 12 % severe, 54% mild, 22% moderate and 12% normal UIE levels (<0.05). Of the total subjects (n=50), 26 women had low levels of FSH. The detection of urinary Daidzein was less (66 %) than Genistein (84%) and reversed trend was observed in FSH reduced subjects who had Daidzein (33%) more than Genistein (15%) (<0.05). HPTLC analysis revealed, Fenugreek (1g) contained 1 mg of Daidzein and Genistein. NHE was provided to these women to consume these food products to bring ameliorating effects on reduced estrogen secretion. Thus, the consumption of these isoflavone rich products proved to be beneficial in combating the hormonal imbalance.

I-47 The NIDCAP ( Newborn Individual Developmental Care Assessment Program )and its significance to improve neurodevelopmental outcome

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With the modern neonatal intensive care survival rate of preterm infants increased dramatically. Concomitant decrease in morbidity has not been documented. In many populations and countries the prematurity rate is increasing. The advanced reproductive technology contributes to the growing number of preterm infants carrying public health significance. Neurodevelopmental outcome of infants at risk for impaired development is concerning. The technically advanced, dehumanized care in the intensive wards poses developmentally unexpected environmental risk for the maturing brain. For preterm infants, the early ,artificial NICU (Neonatal Intensive Care Unit) environment is evolutionarily unexpected. The infants are unprepared for the postbirth adjustment they must make leading to maladaptive development. The NIDCAP (Newborn Individualized Care Assessment Program, H.Als) is based on the synactive theory of development. It provides the framework to conceptualize the organization of capabilities in the early development of the newborn. The NIDCAP assessment needs extensive training and experience. By observing infant behavior before, during and after caregiving thus determining his/her readiness (weaknesses and strengths) and the appropriateness of caregiving and the environment it is possible to give suggestions for his/her care individually - both for parents and staff. Numerous studies support the benefits of NIDCAP care (decreased morbidities, hospital stay, cost, improved growth and neurodevelopment). While it is the standard of care in several countries and numerous NICUs, certain resistance (like with DOHAD) is widely perceived which can be overcome with continuous teaching of parents and staff.
I-48  Efficiency of elimination diet based on results of FED test (Food Environment Drug Test) in pregnant women with allergy

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The aim to estimate efficiency of FED test in pregnant women with allergy during of one year. Material 34 pregnant women with allergy had been included in our research. Middle age made 243,8 year. Methods all patients have been divided into two groups. The first group included 24 pregnant women received elimination diet based on results of FED test. The second group included 10 patients received classical elimination diet by allergy (excluded citrus plants, nuts, eggs, honey, red fish, and seafood’s). Clinical parameters were estimated each month during of one year. Results the main often clinical manifestations of allergy reaction are: dermatitis, nettle rash, itching of skin, rhinitis. The presence of individual food intolerance detect by FED test method. This method can allowing dividing all 100 testable products depending on the degree of expressed a negative reaction on 4 groups (by a heavy, middle, easy degree and neutral). For the patients in the first group the most often intolerance products are: wheat (35%), coffee (30%), kidney bean (28%), cabbage (27%), onion (27%), carrot (25%), beef (23%), reaction on casein (21%), oat (19%). In a first group the clinical manifestations of allergic status became better in a month as compared to a second group. Conclusion FED test is an effective method of correction and treatment of food allergy in pregnant women, providing individual approach in composition recommendations of nutrition for every patient. This method gives proof effect of normalization and stabilization of allergic status after carrying out of research.

I-49  Cow milk allergy and coexisting clinical manifestations

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Introduction: Cow milk allergy is a common gastrointestinal disorder during the first year of life. The incidence of the disease is 0,3%-0,5% and symptoms include systemic, gastrointestinal, respiratory and skin manifestations. Aim: The study of cases exhibiting cow milk allergy during the past two years. Materials/Methods: 31 infants aged 1-12 months, 20 boys and 11 girls, presenting with cow milk allergy, were studied. The diagnosis of cow milk allergy was confirmed by RAST test, an allergen-specific IgE antibody test. The age of onset and the clinical manifestations of food allergy were reported. Results: Within the first 12 months of age, infants developed allergic symptoms (average age of onset age :4 months) and received partially hydrolyzed milk. The percentage of respiratory clinical symptoms, such as persistent rhinitis, otitis and laryngitis was 25,8%(8 infants). 19,3%(6 infants) presented with one episode of bronchiolitis and wheezing, whereas 9,6%(3 infants) with recurrent episodes. 70,1%(22 infants) exhibited emesis/diarrhea and 58,1% (18 infants) bloody diarrheas, either containing mucus or not. Eczema occurred in 77,4%(24 infants) and urticaria in 19,3%(6 infants). Restricted growth exhibited 6,4%(2 infants) and anemia,as unique allergic symptom,3,2%(1 infant). Anaphylaxis was not present in any of the infants. Conclusions: 1.Cow milk allergy is mainly a disease of early infancy and occurs more often in boys. 2.Gastrointestinal symptoms often coexist with respiratory and skin manifestations. 3. The leading symptoms of cow milk allergy are gastrointestinal disorders, whereas anaphylaxis and anemia occur rarely.

I-50  Fetomaternal effects of the carbohydrate metabolism changes in the pregnancy period

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Introduction: We have aimed the fetal and maternal effects by evaluation of the glucose metabolism and glucose tolerance and the determinations of the current values of the defected glucose tolerance. Methods: OGTT is applied by giving 100 g. glucose between the 28-32 gestation weeks of 50 pregnants who haven’t diagnosed as diabetes before. Mothers were divided in to 3 groups according to the second hour glucose levels. The pregnant whose second hour plasma glucose level among 120-164 were defined in the Impaired Glucose Tolerance Test category by NDDG in 1979. Results: LGA which is meaningfully high among the 120- 164 mg / dl glucose values in the second hour was determined ( p < 0,001 ) .The cord insulin level of babies in this group was meaningfully high (p<0,001).OGTT maternal insulin levels of cases that impaired glucose intolerance were determined were high when it is compared to the pregnant in the other group(p<0,05).The high maternal insulin level shows that the periferic insulin level raised. Conclusion:As a result, we informed that the OGTT criterias that O’Sullivan suggested weren’t enough to evaluate the Impaired Gestational Diabetes Tolerance and there should be much more studies to define the standart criterias. In the recent studies, although the criterias which are used for GDM diagnosis, were as the same as NDDG (National Diabetes Data Group) and ADA(American Diabetes Association) criterias, the studies related to impaired gestational diabetes glucose tolerance criterias still go on.

I-51  Using select elimination diet for correction of overweight in Ukraine young people

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Aim: to define the individual select elimination died for weight reduction in young people with overweight during one year. Material: 80 young people had been included in our research with overweight in the age of 202,7 year, men was 32, woman - 48. Methods: we used two programs of nutrition - FED test (Food Environment Drug Test), determined intolerance to 100 foods and carried out selection of products account glycemic index (GI). All patients before the beginning of research and every 3 month measured control weighing, body-mass index (BMI), Brocas index, quantity of fat - device OMRON BF 500. In 32 BMI was within the limits of 26-30, and in 48 - exceeded 30. Results: patients had been distributed on three groups. The first appointed a feed account GI, researched gave out special tables; to the second group had been carried out FED test, researched from the diet excluded intolerable foods for 3 and 6 months; in third group of patients it was carried out FED test with GI. The best results in dynamics in 3 months were observed.
in the second and third groups, in third group weight reduction was much faster and BMI was lower 26 in 65%. After 6 and 9 months there was no increase in weight in patients from the second and third groups. Conclusion: combined use of FED test and selection of products account GI is the most effective and convenient method of reduction and normalization of weight in Ukraine young people with overweight.

I-52 Enteral Glutamine Supplementation in Paediatric Cardiology. A Case Report

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Rationale: Several randomized studies confirm benefits of glutamine supplementation in adult patients however experience in paediatric patients with severe diseases is limited. Methods: This is a retrospective study of a newborn with 3.590 kg of weight and 50cm in length at birth. At the 34th day of life it was diagnosed a non-traumatic chylothorax. At the 24th day of hospitalization the patient began pharmaconnutrition, for adult population, diluted 1:1 for suspicion of intestinal ischaemia. During the five days of administration the formula was diluted to 1:2 and then to 1:3. After this period, he has began a low fat diet through nasogastric tube maintaining total parenteral nutrition which began on the first day of hospitalization. From the 94th day of hospitalization the patient ingested exclusively oral feeding with the introduction of semi-elemental formula. At the 134th day of hospitalization, he was discharged with oral low fat diet adapted to his age and with a body weight of 4.600 kg. Results: After five days of administration of glutamine by enteral nutrition (1 0.6 g/day) there was an improvement in the abdominal clinical condition and decrease of total leukocytes count (18x10^9 9 vs. 15x10^9) and C-reactive protein (1.95 vs. 0.52 mg/dl). Conclusions: Supplementation with enteral glutamine seems to be associated with the maintenance of intestinal function and associated with a decrease in total leukocytes count and C-reactive protein.

II- Epidemiology

II-1 Effects of prolonged and exclusive breastfeeding on maternal adiposity and blood pressure at 11.5 years postpartum: evidence from the Promotion of Breastfeeding Intervention Trial (PROBIT), a cluster-randomized controlled trial.

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Background: Observational studies suggest that a longer duration of breastfeeding helps mothers lose the excess fat they accumulated during pregnancy and may reduce cardiovascular disease risk. Methods: We analyzed data from the Promotion of Breastfeeding Intervention Trial (PROBIT), a cluster-randomized controlled trial involving 17,046 mother-infant pairs at 31 hospitals in Belarus, randomized to usual care (15 hospitals) or to a breastfeeding promotion intervention (16 hospitals). The intervention resulted in substantial increases in breastfeeding duration and exclusivity compared to the control arm (43% vs. 6% exclusively breastfed at 3 months). At 11.5 years postpartum, we measured maternal height and weight, body fat with leg-leg bioimpedance, and blood pressure with an automated sphygmomanometer. We conducted an intention to treat analysis of data collected from the first 8278 mothers followed up, accounting for clustering by hospital. Results: Mean (SD) body mass index (BMI) was 26.8 (5.7) kg/m2, body fat was 33.7 (8.3) %, and systolic blood pressure was 124.2 (14.5) mmHg; 24.5% of mothers were obese (BMI >= 30 kg/m2). The two groups had similar outcome measures, with cluster-adjusted mean differences (95% confidence intervals) for intervention vs. control mothers of -0.34 kg/m2 (-0.97, 0.30) for BMI, -0.36% (-1.11, 0.38) for body fat, and -0.39 mmHg (-3.49, 2.71) for systolic blood pressure. Adjustment for maternal characteristics did not substantially change estimates. Conclusion: We found no evidence that a successful breastfeeding promotion intervention resulted in lower maternal adiposity or blood pressure at 11.5 years postpartum, suggesting that previously reported associations are biased by residual confounding.

II-2 Dietary intakes during pregnancy in Europe - a joint analysis of birth cohort studies: The EARNEST Project

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Background: Although diet during pregnancy may influence reproductive outcomes, little is known about prevailing patterns of intake in industrialized countries, or how diet quality relates to characteristics predictive of pregnancy outcomes. Methods: 12 European countries participated in this collaborative effort to characterize diet during pregnancy. Intakes of fruits, vegetables, meats, seafood and processed meat, and higher seafood intakes. More educated women reported lower red/processed meats and higher seafood intakes in
many countries; they also reported higher intakes of fruits and vegetables, except in several Mediterranean countries with universally high intakes. Overweight (18-41%) was not strongly associated with intakes. Conclusions: Diet quality was markedly poorer among women who smoked during pregnancy, as well as among younger and less educated women. Findings may help maximize the effectiveness of dietary guidelines by targeting these subgroups, and highlight the potential contribution of diet to poor outcomes in these populations.

II-3 Maternal intake of cow’s milk in pregnancy in relation to the offspring’s growth through childhood. Thorhallur Halldorsson1, Camilla Andersen2, Marin Strøm3, Thorkild Sørensen4, Sjúður Olsen4

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Background: Maternal intake of cow’s milk in pregnancy has been associated with both increased weight and length at birth. Tracking this effect into early childhood has, however, not been addressed in detail. Setting: 25,940 mother child pairs from the Danish National Birth Cohort. Analyses were restricted to mothers who gave birth to singleton full term infants, filled out a food frequency questionnaire in mid-pregnancy; and reported their offspring’s length and height measures around 7 years of age. All growth measures where transformed into age and gender specific z-scores. Results: Maternal milk consumption in pregnancy was positively associated (p<0.05) with offspring’s growth measures at birth, age 12 months and 7 years. In comparison to children whose mothers did not drink milk during pregnancy, children whose mothers consumed more than 4 glasses of milk per day had higher adjusted z-scores for birth weight 0.17, (95%CI: 0.06, 0.27) and birth length 0.13 (95%CI: 0.02, 0.24). At 12 months of age, the corresponding z-scores where 0.14 (95%CI: -0.00, 0.28) and 0.12 (95%CI: -0.03, 0.27) for weight and length respectively. At the age of 7 the corresponding difference was 0.10, (95%CI: 0.003, 0.21) for weight and 0.12, (95%CI: 0.02, 0.23) for length, while no differences were observed in the offspring’s body mass index z-scores: 0.06 (95%CI: -0.05, 0.017). Conclusions: The effect of maternal milk intake in pregnancy appears to track beyond the prenatal period, at least up to the age of 7 years. This effect is more dominant for length than for weight for length.

II-4 Characterization of organic food consumers in two major pregnancy cohorts: II Dietary correlates of organic food consumption. Susanne Petersen1, Hamne Torjusen2, Morten Arendt Rasmussen3, Thorhallur Ingi Halldorsson4, Anne Lise Brantsæter2, Magarethaa Haugen2, Helle Margrethe Melzer2, Sjúður Frodi Olsen4

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Background: It is largely unexplored to what extent preferences for organic foods (OFs) in pregnancy may impact offspring health. OFs are lower in pesticides and may be higher in constituents beneficial to health, but women consuming OFs may also have healthier dietary habits in general. We compared dietary profiles of pregnant women with high and low preferences for OFs in two major pregnancy cohorts, the Danish National Birth Cohort (DNBC) and the Norwegian Mother and Child Cohort Study (MoBa). Setting: In DNBC 70,000 and in MoBa 83,000 pregnant women completed a FFQ. The FFQs were similar enabling homogeneous definitions of food-groups across cohorts. Questions about OFs were phrased identically and used to define two groups in each cohort consuming OFs nearly never (DNBC: 7155, MoBa: 33,423) or almost always (DNBC: 4154, MoBa: 1144). Results: Increments in intake (g/day [95% CI]) in always’ v. never’ users were 83.6 [79.9, 87.3] and 45.0 [39.4, 50.5] for vegetables, 12.7 [11.7, 13.6] and 3.9 [2.6, 5.2] for fish, 64.4 [60.2, 68.5] and 87.5 [76.0, 99.0] for fruit, 29.0 [25.8, 32.2] and 17.2 [11.2, 23.2] for dark bread, 11.2 [13.2, -9.2] and -6.8 [-8.4, -5.3] for meat, -16.5 [-18.6, -14.4] and -7.5 [-13.6, -1.5] for white bread, and -33.9 [-43.2, -24.6] (P<0.0001) and -7.8 [-18.0, 2.4] for coffee in DNBC and MoBa respectively. Conclusion: Our findings point to a major challenge in studies examining impact of organic food consumption on health due to potentially irremediable confounding by generally healthier food choices in organic food consumers.

II-5 The effect of birth size on adult blood pressure is modified by salt intake Mia-Maria Peraälä1, Elena Moltchanova1, Niina E Kaartinen1, Satu Männistö1, Eero Kajantie1, Johan G Eriksson2

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Background: Epidemiologic evidence suggests that prenatal growth and nutrition influence adult blood pressure. However, it is unknown whether prenatal growth modifies the association between dietary salt intake and blood pressure in later life. Our aim was to examine the relationship between birth weight and blood pressure response to salt (NaCl) intake. Methods: We studied 2003 participants of the Helsinki Birth Cohort Study, born 1934-44. Information on birth weight was abstracted from birth records. At the study clinic the participants were asked about their medical history and medication. Blood pressure, body weight and height were measured. Diet was assessed with a self-administered, validated food-frequency questionnaire. The relationship between blood pressure and salt intake was tested by a piecewise multivariate regression analysis. Blood pressure was adjusted for sex, age, antihypertensive medication status, gestational age, adult BMI and the reported energy consumption. Results: In those whose birth weight exceeded 3040 g, systolic blood pressure was not sensitive to salt consumption. Among those whose birth weight was below 3040 g, a 1 g higher daily energy-adjusted salt consumption was associated with 3.5% higher blood pressure (p<.005) until the saturation point of 7 g. For diastolic blood pressure, no statistically significant relationship was found. Conclusions: People with small birth weight may be more sensitive to the blood pressure raising effect of salt intake than people with normal birth weight.
II-6 Maternal micronutrient profile and term birth weight: the ABCD cohort study

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Background: Many studies investigate single micronutrients in relation to fetal growth, but nutrients do not occur in isolation. Present study explored the relation of the overall maternal micronutrient profile with indicators of fetal growth. Design: Subsample of the multi-ethnic ABCD cohort: n=3594 women who donated a blood sample for nutrient analyses and delivered a liveborn singleton at term (=37 weeks). Serum concentrations of 25-hydroxyvitamin D, retinol, vitamin B12, folate, ferritin, calcium, zinc, and magnesium were standardized for gestational age at blood sampling (median 13 weeks, interquartile range 12-14) and, for vitamin D, season of sampling. Insufficient levels were defined by the 10th percentile (p10) and summed into a cumulative profile score (range 0-8: 0 if all levels > p10; 8 if all levels < p10). Multivariate regression analyses assessed the relation of the calculated micronutrient profile with birth weight and small-for-gestational-age (SGA) risk. Results: With each additional micronutrient insufficiency, birth weight decreased by -20.5 g (SE 6.0); infants of women with ≥5 insufficiencies (n=109) were on average 129.1 g (SE 47.8) lighter than infants of women without insufficiencies (P<0.05). SGA risk increased accordingly (OR 2.2, 95% CI 1.3-3.6). Results were strongly attenuated by adjustment for maternal ethnicity and associated physiologic factors (parity, age, and height). After additional adjustment for lifestyle and sociodemographic factors, the birth weight difference was -59.2 g (SE 42.7); the OR for SGA 1.3 (95% CI 0.8-2.2). Conclusion: The association between maternal micronutrient profile and fetal growth is largely explained by ethnicity and associated physiologic factors.

II-7 Longitudinal associations between reported sleep duration in early childhood and the development of body composition until age 7

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Introduction: Epidemiological studies in children and adolescents have revealed short sleep duration as a risk factor for weight gain. However, only few studies have addressed sleep in early childhood. Our aim was to determine whether sleep in the second year of life is associated with the development of body composition throughout childhood. Methods: Analysis included 481 DONALD participants with parental reported data on sleep duration and annually measured body composition until age 7. Using median splits of sleeping time at 1.5 and 2 years we defined sleep duration categories: consistently short (CS, n=122), variable (V, n=143) and consistently long (CL, n=216). Polynomial mixed effects regression models were used to analyze differences in the trajectories of Body Mass Index (BMI, kg/m2), Fat Mass Index (FMI, kg/m2) and Fat Free Mass Index (FFMI, kg/m2) from ages 2 to 7 years between the sleep duration categories. Results: Compared to CL-children, CS-sleepers differed in their FMI development with respect to velocity, acceleration and change in acceleration (all p<0.05), resulting in progressively higher FMI levels until age 7. This unfavorable development was pronounced among CS-children, who had been bottlefed or breastfed for ≥2 weeks (p = 0.07 for interaction). Trajectories of BMI and FMI did not differ between the sleep duration categories. Conclusion: Consistently short sleep duration in the critical window of early childhood appears to adversely affect the development of body fat until age 7.


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It has been suggested that restricted intrauterine growth may lead to higher disease risk via accelerated postnatal growth. This study evaluates the associations between prenatal maternal factors, birth length (BL) and infant peak height growth velocity (PHV) in two longitudinal population-based birth cohorts born 20 years apart. The study consists of singletons from the prospective Northern Finland Birth Cohorts 1966 (NFBC1966, N=3,783) and 1986 (NFBC1986, N=5,577) with frequent height measurements at 0-2 years. Reed1 model was used to estimate individual height growth curves by sex. PHV was derived as the maximum value of the growth velocity curve. Its association with BL and maternal factors was studied using unadjusted and adjusted regression models by cohort and sex, after filling in missing values by multiple imputation method. The mean PHV was 53 cm/year in both cohorts, 3-4 cm higher in boys than in girls. We identified an inverse association between BL and log-transformed PHV, which was much stronger in the NFBC1986 (-2.6%/cm) than in the NFBC1966 (-0.3%/cm), possibly partly due to the improvement of accuracy of BL measurements over 20 years. Maternal height showed a positive, presumably genetically mediated association with PHV. Parity showed an inverse PHV association, which remained virtually unaffected after adjustment for other factors. Pre-eclampsia was associated positively with PHV in NFBC1966 males and NFBC1986 females. Maternal education, smoking and BMI were not associated with PHV. This study supports the hypothesis that smaller size at birth is associated with accelerated postnatal growth, independently of confounding factors.

II-9 Exposure to Maternal Depression Early in Life and Patterns of Weight Gain in Latino Children

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Background: Exposure to maternal depression in utero and in the postpartum period may impact the future course of child weight gain. Objectives: To evaluate the relationship between exposure to perinatal depression and infant weight gain in Latino infants, a group at high risk for future overweight. Methods: Latina mothers were recruited prenatally and followed until the children reached 24 months of age. At 6, 12 and 24 months, the infants were weighed and measured, the infants were weighed and measured and the infants were weighed and measured. Additionally, maternal depressive symptoms were assessed prenatally and...
at 4-6 weeks postpartum. Mixed logistic and mixed models were used to assess independent predictors for weight/height Z scores, risk for overweight (defined as >85th percentile weight/height) and risk for underweight (<5th percentile weight/height) in the first 2 years of life. Results: We enrolled 201 mother-infant pairs. At 12 months, 27.6% of infants were overweight at and 2 years 39.9% were overweight. Infants exposed to maternal depression in the prenatal and at the postnatal period had a lower weight/height Z scores (-0.44, 95%CI (-0.83--0.04) after controlling for breast-feeding and also were more likely to be overweight (OR 5.19, 95%CI 1.75-15.34) and less likely to be overweight (OR 0.31, 95%CI 0.11-0.89) in comparison with unexposed infants or those exposed only prenatally or postnatally. Conclusion: Exposure to maternal depressive symptoms perinatally is associated with reduced infant weight gain, reduced risk for infant overweight and increased risk of underweight in comparison with infants not exposed to maternal depression or those exposed only episodically.

II-10 Chronic disease and late life morbidity and mortality among Finnish children who were evacuated without their parents during World War II

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Objective: To study cardiovascular disease morbidity and mortality 60 years after exposure to a traumatic separation in early life due to World War II.

Methods: The epidemiological study cohort consists of 13345 people who were born 1934-1944 in Helsinki. One major exclusion criteria was moving away from Finland. This study includes 11862 subjects of whom 1505 (13.0%), were former war evacuees. The data on evacuations was extracted from the Finnish National Archives. Information on childhood socioeconomic status, based on the father’s occupation. Morbidity of cardiovascular disease was based on information from the national register of medication reimbursement, the Finnish Hospital Discharge Register and the Causes of Death Register. The register data was adjusted for gender and date of birth. Results: Prevalence of coronary heart disease was higher among former war evacuees (8.2% vs. 4.8%; Odds ratio (OR) = 1.3, 95% confidence interval [95% CI], 1.1 to 1.7; P = 0.009). The same trends of prevalence rates were seen according to high childhood socioeconomic status (6.9% vs. 3.0% HR = 1.3, 95% CI, 1.0 to 1.6; P = 0.037). A relationship between evacuation and all-cause mortality (17.2% vs. 13.6%; HR = 1.1, 95% CI, 1.0 to 1.3; P = 0.069) was also observed. Conclusion: People who were separated from their parents in childhood have higher rates of coronary heart disease in adulthood. The evacuation in childhood also predicts higher overall mortality. This longitudinal study setting is among the first to show that adverse childhood experience influence cardiovascular disease risk later in life.

II-11 IGF-I and insulin in healthy Danish infants (the SKOT cohort); relations to diet and anthropometry.

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Background: Diet and high growth velocity during early childhood can be risk factors for overweight and metabolic syndrome. Our cohort investigates the effect of early nutrition on growth and risk factors for later disease. Objective: To better understand the complex interaction between diet, IGF-I, insulin and growth. Design: Analysis of data from blood sampling and diet at 9 months and anthropometry up to 18 months from 312 singleton term infants. Results: Infants partially breastfed at 9 months (54%) had lower median insulin (p=0.042) and IGF-I concentrations (p=0.0005), than those not breastfed. Furthermore, there was a highly significant negative dose-response relationship between number of breastfeeding per day and both IGF-I (p=0.0002) and insulin (p=0.0004). Among those not breastfed current formula intake was not correlated to insulin and IGF-I but positively correlated with free IGF-I (IGF-I/IGFBP3, p=0.03). Insulin and IGF-I values were correlated (r=0.22, p=0.0003) and both were positively associated with change in weight-for-age Z-score 5-9 months. When comparing IGF-I values with growth from 9-18 months there was a positive association with linear growth and no association with weight gain. Interestingly, IGF-I was negatively associated with change in BMI. Conclusion: We expected the positive association between current weight gain and IGF-I and insulin, but was surprised to find that intensity of breastfeeding has such strong endocrine effects during complementary feeding. It is interesting in relation to early obesity that high IGF-I at 9 month was associated with less increase in BMI during the following 9 months, but it needs further exploration.

II-12 Fetal nutrition, as reflected by birth weight, may have a programming effect on lepton levels.

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Background. The hormone leptin, mainly produced in the adipose tissue, is involved in the regulation of body weight. The release of the hormone is increased in obese persons. This study investigated whether the plasma leptin level in adolescents was related to the infant’s birth weight (BW). Methods. The present study comprised 677 (396 females) adolescents aged 12.5-17.5 years from the HELENA study. Neonatal data were obtained from parental records. We measured weight, height and total adiposity (sum of 6 skinfold thicknesses) and fasting plasma leptin levels. Results. Mean birth weight for boys and girls was respectively 3.44 (0.58) kg and 3.30 (0.52) kg (p=0.001) and mean sum of skinfolds was respectively 74.4 (40.3) mm and 100.3 (37.5) mm (p=0.001). Mean leptin levels for boys and girls were respectively 9.3 (4.9) ng/ml and 28.3 (25.6) ng/ml (p=0.001). Birth weight was negatively associated with plasma leptin level in adolescents (B = -0.113, p < 0.001) after adjusting for gestational age, current age, pubertal status and the sum of six skinfold thicknesses. However, when analyzing boys and girls separately, this relationship remained only significant for girls (B = -0.086; p=0.003), while not for boys (B = 0.047; p=0.180). Conclusions. Our study shows an inverse association between BW and
plasma leptin levels in female adolescents, independently of adiposity and other potential confounders. These findings suggest that fetal nutrition, as reflected by BW, may have a programming effect on leptin levels. Key words: adolescent, leptin, birth weight.

II-13 Dietary exposure to benzo(a)pyrene (BaP) during pregnancy, GSTP1 polymorphisms and birth weight
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OBJECTIVE: This study aimed to assess associations between maternal dietary exposure to benzo(a)pyrene (BaP) during pregnancy and birth weight, and examine whether associations differed by polymorphisms in the GSTP1 (glutathione S-transferase pi 1) gene, involved in detoxification of xenobiotic compounds. METHODS 657 women from the Spanish ‘INMA’ (Environment and Childhood) cohort from Sabadell (Barcelona) were recruited during the first trimester of pregnancy. Dietary exposure to BaP was estimated from food consumption data. Genotyping was conducted for the coding variant Ile105Val from GSTP1 in mothers and children. Multivariable linear regression was used to assess the association between birth weight and BaP intake, stratified by GSTP1 polymorphisms. Preterm births were excluded. RESULTS Mean birth weight differed significantly by BaP intakes (3301.9g in the 1st quartile vs. 3190.7g in the 4th quartile). Overall, BaP intakes were associated with lower birth weight after adjusting for potential confounders. The mean birth weight was 14161g lower for the 4th vs. 1st quartile of dietary BaP. No effect of BaP exposure on birth weight was found among subjects with maternal or infant Ile/Ile GSTP1 genotype related with high detoxification enzyme activity. However, the mean birth weight was about 200g lower for the 4th vs. 1st quartile of BaP intake among those with maternal or infant GSTP1 genotype associated with lower detoxification enzyme activity (Ile/Val or Val/Val: 20095 and 19795g, respectively). CONCLUSION Dietary intakes of BaP were associated with lower birth weight. GSTP1 Val-105 allele may result in greater susceptibility to adverse effects of dietary BaP on birth weight.

II-14 Early introduction of fish decreases the risk of allergic rhinitis in preschool age
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OBJECTIVE: This study aimed to analyze factors for allergic rhinitis at preschool age. Methods: Data were obtained from a longitudinal study of a cohort of children born in Western Sweden in 2003. 8176 families were randomly selected. The parents answered questionnaires at 6 and 12 months and at 4.5 years of age. The response rate at 4.5 years was 4946, i.e. 83% of the 5398 questionnaires distributed at 4.5 years. Results: At 4.5 years of age, 5.5% reported symptoms of allergic rhinitis during the last year (current). 1.7% reported doctor-diagnosed allergic rhinitis with symptoms during the last year. In the multivariate analysis risk factors for current allergic rhinitis were: family history of rhinitis, male gender, own eczema or doctor-diagnosed food allergy during the first year and antibiotics in the neonatal period (OR 1.8; 95% CI 1.02-3.2). Fish before the age of 9 months decreased the risk (OR 0.6; 0.4-0.9). Independent risk factors for doctor-diagnosed allergic rhinitis were: family history of rhinitis (OR 2.7; 1.4-5.4), male gender (OR 2.1; 1.1-4.1), own eczema (OR 2.9; 1.6-5.3) or recurrent wheeze (OR 3.2; 1.5-6.9) during the first 12 months. Conclusion: Introduction of fish before the age of 9 months decreased the risk of allergic rhinitis in preschool age. Family history of rhinitis, male gender, own eczema or recurrent wheeze in the first year, as well as neonatal antibiotics, increased the risk.

II-15 The role of infant feeding in explaining ethnic differences in early growth
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Objective: Early rapid growth may influence later development of overweight and cardiovascular disease, which disproportionally affects ethnic minorities. We determined ethnic differences in growth velocity (standard deviation scores, sds) during the first 6 months of life and the explanatory role of infant feeding. Methods: Data were derived from a multi-ethnic cohort in the Netherlands (ABCD study). Pregnancy outcome and growth data (weight and length) of 3904 singleton infants were available for eight ethnic populations: Dutch (n=1971), Surinamese-Hindustani (n=68), Surinamese-Creole (n=146), Antillean (n=50), Turkish (n=222), Moroccan (n=343), Ghanaian (n=79), and other non-Dutch countries (n=1025). ?sds-weight, ?sds-length and ?sds-weight-for-length between 4 weeks and 6 months were defined using internal growth references. We examined the contribution of infant feeding (breast-, bottle- and complementary feeding) on ethnic differences in growth velocity with multivariate linear regression. Results: Growth velocity was higher in all non-Dutch groups varying between 0.22 to 0.61 for weight (Dutch: -0.15) and 0.18 to 0.70 for length (Dutch: -0.06). Growth velocity in weight-for-length was similar across groups, except for the Moroccan children (0.44, P<0.05). Differences remained significant upon adjustment for confounders. Children of African descent were breastfed shorter and bottle feeding and solid foods were introduced earlier, which explained partly the higher growth in weight and length in these groups. Conclusion: Ethnic disparities in early infant growth are to a small extent explained by differences in infant feeding pattern. More research is needed to explore the unbalanced growth in the Moroccan group and the underlying factors of rapid growth in general.

II-16 Long-term modulation of enzyme activity in fatty acid metabolism by breastfeeding.
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Background: The nutritional environment during early infancy may have long-term physiologic effects in humans by means of early
life programming. Long chain polyunsaturated fatty acids (LCPUFA) play important roles in neurological development and protection against cardiovascular disease. These fatty acids are synthesized from essential fatty acids by alternating steps of desaturation and elongation. Objective: To examine whether enzyme activity in adolescence, derived from serum fatty acid profile, is related to breastfeeding. Methods: Serum fatty acid profiles were examined in 887 adolescents (56% females) aged 14.7 + 1.2 years. Adolescents born at less than 35 weeks of gestational age were excluded. Enzyme activities were calculated by dividing amounts of products by amounts of precursors. Information on birth weight, gestational age and breastfeeding duration were obtained from parental records. Results: Results indicate a positive association between breastfeeding duration and the activity of the enzyme Elongase in adolescence. A significant (P = 0.040) association is found when correcting for possible confounders, such as pubertal status, age, sum of six skinfold thicknesses, birth weight and usual dietary intake of fish. However, when analyzing boys and girls separately, we found a highly significant correlation for boys (p = 0.003) while not for girls (p = 0.474). No correlation was found for any of the desaturating enzymes. Conclusion: These results confirm previous findings that total polyunsaturated fatty acid concentrations are higher in adolescents that were breastfed. Further research is needed to investigate this correlation that is found only in boys.

II-17  Influence of parental socioeconomic characteristics, child health and physicians’ advice on the choice of infant formula-milk - Results from EDEN mother-child cohort study (study of pre and early postnatal determinants of the child’s development and health).

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Objective: To determine the influence of parental socioeconomic characteristics, child health and physicians’ advice on the choice of infant formula-milk. Methods: Data from 1908 newborns were collected in the EDEN study. From this sample, 477 infants exclusively fed with formula-milk during the first 4 months were selected. Our analysis focused on 300 subjects with data on the different types of formulas used from birth (regular, hypoaallergenic, enriched, enriched in probiotics). Subjects were considered as consumers if they had been exposed at least a week to the considered formula. Three groups of explanatory variables were used: child health (diarrhea, regurgitation, colic, eczema), parental characteristics (marital status, income, history of allergies) and type of physicians (general practitioners, specialists) in multivariate logistic regressions with type of formula as dependent variable. Results: Regular formulas were more prescribed by general practitioners than by other physicians (p<0.0001); they were less often consumed by infants suffering from colic (n=116, p=0.01). Consumption of hypoallergenic formulas was associated with recruitment center (p=0.03) but not to parental history of allergies (p=0.22). Consumption of thickened formulas was positively associated with parental history of allergies (p=0.02) and occurrence of regurgitations (p=0.01). Consumption of enriched probiotics formulas was positively associated with the fact that mothers were living alone (p=0.02), with the occurrence of regurgitations (p=0.001) and negatively with the occurrence of eczema (p=0.02). The type of formula was not related to parental income (all p>0.20). Conclusion: These results suggested that the choice of infant formula was more influenced by health’s events of infants and the type of physician consulted than by parental socio-demographic characteristics.

II-18  Early postnatal growth and blood pressure in young rural adults from India - Pune Rural Cohort.

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Evidence that reduced fetal growth increases risk for adult diseases is accumulating but that in case of early postnatal retarded growth is scanty. Since growth faltering in first two to three years is prudent in developing countries, its long term consequences may have strong impact on adult health in such populations. Rural adults (males 386 & females 223) who were also studied during their preschool age were measured for anthropometry and blood pressure. Prevalence of stunting (Z score < -2) in 3-5 yr age was high (over 50%) but that of adult adiposity was low (5 - 7 %) in both sexes. Results: Early postnatal growth retardation also confers risk for adult non communicable diseases (p<0.00), adult leg height (p<0.00) but not body mass index (BMI). Among stunted subjects especially males, both mean systolic (SBP) and diastolic blood pressure (DBP) increased (by 10 mmHg and 5 mmHg respectively) significantly (p<0.00) from lower to higher tertile of adult BMI. However, similar trends were not seen among non stunted subjects. Multiple regression analysis showed that stunting at 3+ yr had independent effect (β = 3.43, p<0.05) only on DBP after adjusting for adult BMI. Further, logistic regression showed significant risk for high DBP (OR: 3.836, 95% CI: 1.5-9.6) among stunted group considering non stunted group as reference category. Our results suggest that early postnatal growth retardation also confers risk for adult non communicable diseases in undernourished populations.

II-19  Lower maternal folate status in early pregnancy is associated with childhood hyperactivity and peer problems in offspring

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BACKGROUND: Maternal nutrition during pregnancy has been linked with fetal brain development and psychopathology in the offspring. We examined for associations of maternal folate status and dietary intake during pregnancy with brain growth and childhood behavioural difficulties in the offspring. METHODS: In a prospective cohort study, maternal red blood cell folate (RCF) was measured at 14 weeks of pregnancy and total folate intake (TFI) from food and supplements was assessed in early and late pregnancy. The offspring’s head circumference and body weight were measured at birth and in infancy, and 100 mothers reported on children’s behavioural difficulties at a mean age of 8.75 years using the Strengths and Difficulties Questionnaire. RESULTS: Lower maternal RCF and TFI in early pregnancy were associated with higher childhood hyperactivity (RCF: beta = - .24, p = .013; TFI: beta = - .24, p = .022) and peer problems scores (RCF: beta = -.28; p = .004; TFI: beta = -.28; p = .009) in the offspring. Maternal gestational RCF was positively associated with head circumference at birth (adjusted for gestational age), and mediation analyses showed significant inverse
II-20  Association of metabolic syndrome in early pregnancy with measures of adiposity in neonates
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OBJECTIVE: Growth trajectories leading to obesity may begin in utero and continue in early childhood. The purpose of this study was to determine the association between components of metabolic syndrome in early pregnancy (12 weeks of gestation) and measures of body fat in newborns participating in the mother-child cohort study (Rhea study) in Crete, Greece, 2007-2009. METHODOLOGY: At the time of the first major ultrasound examination (mean: 12 weeks), maternal fasting serum samples were collected and blood pressure was measured. Skinfold thickness, weight, length and abdominal circumference were measured at birth for 163 newborns. Multivariable linear regression models were used. RESULTS: Mean concentrations in the first trimester were 80.1 mg/dl for glucose, 212 mg/dl for total cholesterol, 66 mg/dl for HDL, 123 mg/dl for LDL, and 115 mg/dl for triglycerides. Maternal obesity (BMI pre-pregnancy> 30 kg/m2) was significantly associated with BMI in neonates (coefficient: 0.6, 95%CI: 0.1.1.1) and abdominal circumference (coefficient: 0.2, 95% CI: 0.02,1.8) at birth, after adjusting for maternal age, education, parity, infant gender and gestational age. A per unit increase in the LDL/HDL cholesterol ratio was significantly associated with increased body fat percentage in neonates (coefficient: 1.0, 95%CI: 0.2,1.9), likewise an elevation of 10 mg in systolic and diastolic blood pressure in early pregnancy was associated with increased abdominal circumference at birth (coefficients: 0.6 95%CI: 0.2,1.0 and 0.5, 95%CI: 0.01,0.9 respectively). CONCLUSION: The results suggest that metabolic syndrome in early pregnancy is a risk factor for increased body fat measurements at birth.

II-21  Validation of a food pictures atlas to assess children dietary intake
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Introduction: Within the EU Childhood Obesity Project (EU CHOP) a 3-day food diary has been used to assess children’s dietary intake. The estimation of the consumed portion size by participants is the main difficulty in the evaluation of their dietary intake when a scale can not be used (i.e. meals prepared out of home). To solve this problem, a short food pictures atlas (FPA) has been developed. Objective: To validate a FPA as a tool to estimate food portions in the Spanish CHOP sample. Methods: Cross validation study with mothers and fathers of preschool-age children taking part in EU CHOP. Participants estimated the portion of 24 pre-weighted exposed dishes, and 12 dishes served by themselves, using the FPA. The accuracy in the evaluation of each dish was classified by means of the variable ‘estimated weight - real weight’ (EW-RW). After assessing each variable normal distribution, Pearson correlations were applied between EW and RW. Bland and Altman plots were generated to validate the estimation of each dish. Results: A total of 59 mothers and fathers participated in the validation study. The 74% of the dishes were classified in the optimal (maximum 10% error) and acceptable (10-25% error) accuracy groups. All the portion estimations correlated significantly with their real weights obtaining r values between 0.33 and 0.90. Bland and Altman graphics showed a good precision. Conclusions: This tool allows a correct estimation, up to 74%, of food portions. This food atlas is a useful aid tool to assess dietary intake in pre-school children.

II-22  Definitions of childhood obesity and the effect of different classifications on long-term outcomes
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High body mass index (BMI) in childhood may have long-term consequences. However, trends and comparisons in the prevalence of childhood obesity are difficult to quantify due to a variety of definitions. In a birth cohort, the effect of different classifications of overweight and obesity (WHO Z-score >+2.0 and >+3.0 and IOTF cutoffs) on long-term outcomes was assessed. In 1982, 5,914 children born in Pelotas (Southern Brazil) were included in a cohort study. In 2004-5, 4,297 cohort members were interviewed and blood samples were collected in 90% of them. Nutritional indices obtained at ages 4 and 23 years were analyzed through correlations coefficients and kappa. The analyses were also focused on the sensitivity and positive predictive value (PPV) of different classifications of obesity in childhood and adverse outcomes in adulthood. Correlation between z-scores of weight-for-height and BMI-for-age was 0.99 and Kappa index was 0.93 using >+2 Z-score as cutoff. Overweight and obesity defined by IOTF criteria showed higher sensitivity for overweight (29.5%) and obesity (43.6%) in adulthood. However, the predictive capacity of WHO was higher than IOTF criteria (PPV = 66.1% for overweight and PPV = 41.1% for obesity). For the other outcomes in adulthood, the sensibility of IOTF was higher for high waist circumference (39.8% in men and 32.2% in women), while the PPV of WHO was higher than IOTF was higher for waist circumference (50%) and high blood pressure (28.5%) in men. The best predictive capacity, in women, was observed for the IOTF on high waist circumference in adulthood (PPV = 25.4%).

II-23  Determinants of infant n-3 LCPUFA status and its associations with blood pressure and lipid profile
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Objective: Infant n-3 long-chain polyunsaturated fatty acid (LCPUFA)-status in erythrocytes (RBC) is influenced by intake of n-3LCPUFA from complementary food, breast milk and intrauterine nourishment. However, few studies have investigated the degree of influence conferred by determinants of n-3LCPUFA-status or effects of n-3LCPUFA-status on blood pressure (BP) and lipid profile in a cross-sectional design. Procedure: We performed a cross-sectional study with 466 healthy Danish 9 month-old infants to investigate
dietary determinants of n-3LCPUFA-status and its associations with BP and lipid profile. We assessed if they were still breastfed (BF), if fish had been introduced, RBC fatty acid composition, BP and plasma concentrations of LDL-C, HDL-C and triacylglycerol. Results: The RBC content of n-3LCPUFA was 9.62.3 FA% (mean±SD) (range: 3.3-17.3 FA%). 23% of the variation in n-3LCPUFA-status was explained by infant age (p=0.003), maternal smoking during pregnancy (p=0.006), BF (p=0.001) and fish introduction (p=0.033). Infant age and maternal smoking were positively and negatively associated with n-3LCPUFA status, respectively. BF and fish introduction conferred a 19% and 16% higher status, respectively. They did however tend to interact (p=0.073) and a significant association between fish introduction and n-3LCPUFA-status was found only among non-BF infants (p=0.003). Inclusion of maternal fish intake (p=0.001) in a sub-analysis (28% of the infants) further increased the explained variation to 36%. n-3LCPUFA-status was not associated with BP or lipid profile. Conclusion: Breastfeeding and introduction of fish are equally important determinants of n-3LCPUFA-status in 9 month-old healthy Danish infants. Associations between n-3LCPUFA-status and BP or lipid profile were not found.

II-24  Protein intake and growth in the latter half of the first year of life
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Background: A study on Icelandic infants conducted in 1995-1996 showed that protein intake was too high. Following that study recommendations on infant nutrition were revised. Protein reduced cow’s milk was recommended instead of normal cow’s milk from 6-months-2 years of age and recommendation on exclusive breastfeeding was prolonged to 6 months instead of 4-6 months previously. Objectives: To evaluate if new recommendations had any effect on the protein intake and growth. Furthermore, to investigate if protein intake had any influence on growth. Design: A longitudinal observational cross-sectional study. Randomly selected healthy term Icelandic infants (n=196) born in 2005 were investigated until 12-months old. Dietary data were collected by dietary-histories for 0-5-month-olds and monthly registrations for 5-12-month-olds. Anthropometric measures were regularly registered. Results: Compared to the previous infant study the velocity of weight growth from 6-10 months was significantly lower in infants born 2005 (p=0.008). Protein intake among girls was significantly lower in the present study compared to the prior study. Protein intake as a percentage of total energy was also significantly lower in the present study than in prior study. Furthermore, protein intake (g/kg) among 9-month-olds was positively related to weight growth velocity from 8-12 months (r=0.204, p=0.019). Conclusion: Protein intake has lowered since the prior study, but still exceeds recommendations. The reduction in velocity of weight growth might be the result of reduced protein intake and higher breastfeeding rates in the later half of the first year. Decreasing the protein intake further could be gained through increased breastfeeding.

II-25  Emotional problems in adolescence and metabolic syndrome in mid-life: the modifying effect of C-reactive protein (CRP) gene
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Depression is associated with the development of the metabolic syndrome (MetS) and both disorders with markers of systemic inflammation, such as C-reactive protein. We examined associations between emotional problems (depression/anxiety) at age 13-15 years and MetS at age 53 years in a large representative British birth cohort. We also investigated whether two CRP polymorphisms (rs1205 and rs3093068) were associated with emotional problems and the MetS, and whether the risk of the MetS in those with emotional problems was modified by CRP gene. Those with depression/anxiety in adolescence (OR=1.30, 95%CI: 0.98, 1.74) were more likely to have the MetS. This association was stronger in women than in men. Although CRP gene was not associated with emotional status or the MetS, the association of adolescent emotional problems with the MetS was stronger in those who were homozygous for the major allele (C) of rs1205 (OR=1.83, 95%CI: 1.17, 2.86) than in carriers of the T allele (OR=1.01, 95%CI: 0.66, 1.55) (p=0.05 for gene by emotional status interaction). Adolescent-onset depression and anxiety may play an important role in the MetS risk later in life, particularly in those homozygous for the major allele of CRP rs1205. These findings may highlight new ways of identifying depressed people at high risk of developing the MetS, which is of great importance for the treatment and clinical management of depressive patients.

II-26  Determinants of breast-feeding in a southwestern Swedish cohort
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Breast-feeding has important health benefits. To promote breast-feeding it is essential to determine why mothers choose to breast-feed. The aim of this study was to assess which factors have an impact on breast-feeding at one month. Method: The study is a population-based longitudinal cohort study that recruited infants between 1 October 2007 and 31 December 2008. 3860 families were invited and of these, 2672 families were included (69.2%). Results: At one month 74% of the infants were exclusively breast-fed, and only 1.5% exclusively formula fed. One out of five breast-fed 10 times/day or more and 43.4% reported breast-feeding problems. Factors positively associated with breast-feeding at one month were high parental education and mothers born in Sweden. Breast-feeding problems, use of pacifier or thumb sucking showed a negative association. This was also found with maternal smoking, preterm birth, low birth weight and admission to neonatal ward. In a multivariate analysis we found that the likelihood for a successful breast-feeding increased if the mother received the main breast-feeding support from the maternity ward (2.19; 1.27-3.78) or the Child Health Care Centre (CHC) (Odds ratio 3.53; 95% confidence interval 1.22-10.22). Negative factors were low maternal education (0.52; 0.31-0.88), preterm birth (0.49; 0.24-0.99) and breast-feeding problems (0.09; 0.04-0.18). Conclusion: We found that support from the maternity ward or the CHC were important independent positive factors for breast-feeding at one month of age. Negative factors were low maternal education, preterm birth or breast-feeding problems.
II-27  Thinness at birth is associated with low HDL cholesterol and high triglyceride levels in late adolescence; the Copenhagen Cohort Study
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Background: It has been hypothesized that size at birth and growth in infancy may programme future propensity to adult diseases such as metabolic syndrome (MS). Thinness at birth measured as ponderal index (PI) and low birth weight reflect poor fetal nutrition that may cause long-term adaptation of the metabolism, but studies on contemporary cohorts with normal birth weight are limited. Objective: To investigate associations between size in infancy and markers of MS, i.e. insulin resistance, lipid profile and blood pressure (BP) at 17-year. Method: 103 healthy term infants with normal birth weight from this prospective observational cohort participated. Anthropometry was measured at birth and 9 months. Follow-up examinations at 17-year included anthropometry, blood sampling and BP measurement. Results: PI at birth was positively associated with HDL-cholesterol (βSE = 0.0350.014, P=0.013) and negatively with triglycerides (βSE = -0.0550.024, P=0.022), respectively, adjusted for gender and independently of current BMI, birth weight, size at 9 mo and duration of breast feeding. PI at birth was not associated with LDL-cholesterol or BP. However, insulin resistance measured as HOMA index was negatively associated to BMI at 9 mo (βSE = -0.2090.093, P=0.026) adjusted for gender and current BMI, but dependent on one case with current BMI=37kg/m2. Birth weight or PI at birth was not correlated to HOMA at 17-year. Conclusion: Moderate thinness at birth, but not birth weight, was associated with an adverse altered lipid profile in late adolescence in this cohort with normal birth weight and a low prevalence of overweight at 17-years.

II-28  Protein intake by breast-fed and bottle-fed infants of first three months of life in Russia
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It is proposed that excess of infants’ food protein intake may be one of the risk factors of obesity, diabetes and metabolic syndrome. The protein intake in bottle-fed infants is rather well known, however these data on breast-fed infants are scarce. The main problem of breast-fed infants’ protein intake study is the exact evaluation of daily milk consumption. The aim of study is to compare protein consumption by breast-fed and bottle-fed infants measuring the exact daily milk intake. Methods. The milk volume consumed, body weight and milk protein content were measured in 110 breast-fed infants of three months of life. The volume of market available infant formula consumed and body weight were measured in 90 bottle-fed infants of the same age. Breast milk intake was measured by weighing of infants before and after each feeding during a day. Breast milk and formula protein content were measured by Kjeldal method. Results. Average breast milk volume consumed at one month of life was 78520, at 2 months - 89835 and at 3 months of life - 91229 ml/day, and the average protein intake - 2.08; 2.60 and 2.32 g/kg/day respectively. Conclusion. Our data show that protein intake by Russian bottle-fed infants is higher than that one of breast-fed infants and confirm the tendency showed in other countries.

II-29  Long-term effects of the perinatal environment on lipid metabolism and body composition.
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Introduction: Recent studies have indicated that preterm infants are prone to the adult metabolic syndrome. Our question is how early dose it start. Since some of school children who haddischarged NICU underwent a health examination at 10 and/or 13 years old in our city, we investigated the correlation between prematurity and the metabolic syndrome of childhood. Objectives: To ascertain their correlation to gestational age (GA) or extrauterine growth restriction (EUGR) and the metabolic syndrome of childhood. Methodology: Data collection from neonatal files from January 1990 to December 1998 and health evaluation of these children at 10 and/or 13 years old. 53 children were available for assessment. Sample numbers were so small that we subdivided the population into two groups which are GA<34, >73 weeks. We collected the data of height, weight, body mass index (BMI), blood pressure, serum total cholesterol (T-CHO), HDL, LDL, TG, and GPT from health examination. We compared these data with GA and EUGR. Statistic analysis by JMP (7.0.2). Results and Discussion: GA<34 weeks group showed higher T-CHO and LDL than >34 week group. These findings indicate that prematurity is a high risk of a lipid metabolic abnormality and this propensity has already started in childhood. EUGR group significantly showed lower BMI and higher serum LDL than non-EUGR group at 13 years old. This means EUGR group could be a candidate to the cardiovascular disease. Conclusion: Prematurity is a high risk factor for the metabolic syndrome. We should continue tight follow-up for these preterm-children.

II-30  Impact of wheat flour fortification with electrolytic elemental iron on the prevalence of iron deficiency anaemia among women at childbearing age and preschool children in Morocco
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Background Iron-deficiency anaemia is a major nutritional problem in Morocco where it affects 32,6 % of females at reproductive age and 31,5 % of preschool children. A programme of wheat flour fortification with electrolytic elemental iron and B-vitamins was launched. Objectives. To evaluate the impact of wheat flour fortification with electrolytic elemental iron on iron status of women of childbearing age and preschool children. Methods two surveys were conducted. A total of 268 and 130 women were studied in may 2006 and December 2007, respectively. 146 and 201 children were recruited in may 2006 and December 2007, respectively. Haemoglobin, plasma ferritin and C-reactive protein were analysed. Results. The prevalence of anaemia in women was 33,6 % and...
36.7% in May 2006 and December 2007, respectively. The prevalence of iron deficiency anaemia in women was 21.5% and 21.7% in May 2006 and December 2007, respectively. The prevalence of anaemia among preschooler children was 32.2% and 31.6% in May 2006 and December 2007, respectively. The prevalence of iron deficiency anaemia in preschool children was 5.4% and 5.1% in May 2006 and December 2007, respectively. Conclusion results show a slight improvement of iron status in women of childbearing age and preschool children. This is probably due to insufficient coverage of fortified flour throughout the country. Indeed, only 32.7% of the flour was fortified. Thus, this evaluation should be carried out again once total industrial flour is fortified. Key words: anaemia, iron deficiency anaemia, preschool children, women of childbearing age.

II-31 The Effect of Diet on the Mental Performance of Children; the Nutrimenthe project.
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Abstract submitted by Claire Horton on behalf of the Nutrimenthe consortium.

There is evidence to suggest that diet can affect the mental performance (MP) of children. Nutrimenthe (FP7 project: 212652) aims to improve understanding of this through epidemiological studies and randomised nutritional intervention trials of specific nutrients (including B-vitamins, minerals, protein and LC-PUFAs) introduced during pre-natal and early post-natal development with MP being assessed through a battery of neuropsychological tests harmonised for use by Nutrimenthe. Additionally, Nutrimenthe is assessing parents’ knowledge of the role of diet on MP and is assessing the economic impact of improving MP. Results: Fish eating was positively associated with levels of EPA & DHA during pregnancy and in the child at birth. Inadequate folate acid supplementation during early pregnancy is related to toddlers showing behavioural problems at 18 months. Intervention studies during childhood may have a positive effect on MP. Early nutrition will impact on some genetic polymorphism expression which may effect, in the long-term, MP and behaviour. Verbal learning was analysed in a randomised intervention trial of B-vitamin or placebo, using a cognitive test battery. Parents are concerned with balancing the provision of a nutritious diet with satisfying their children’s food preferences as developing good eating habits could have long term health implications. High treatment costs for lower mental development and mental disorders could be saved for society. Conclusions: Nutrimenthe will allow assessment of the: effect of several nutrients on MP in children, attitudes of consumers to diet and MP and cost impact of improving mental performance.

II-32 Mothers’ Food Consumption and Lifestyle during Pregnancy and Birth Weight of Their Infants
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Data indicate that low birth weight and rapid infant catch-up growth as well as high birth weight may play a significant role in the risk of developing overweight, type 2 diabetes and the metabolic syndrome later in life. This study investigated 169 women during pregnancy and the birth weight of 172 (3 twin births) newborns in Burgenland, Lower Austria and Upper Austria. Participants were 295 years of age. The majority of women had as highest education level a graduation from apprenticeship training. Maternal lifestyle factors, especially eating patterns, influence intrauterine fetal growth. Beside gestational age and birth weight related to gestational age, birth weight is the most used instrument to define morbidity and mortality risks of newborns. Scientific data show evidence that the intake of specific fatty acids and vitamins (A, B6), maternal diseases (hyperemesis gravidarum, diabetes), and maternal lifestyle factors (consumption of nicotine, caffeine, alcohol, as well as physical activity, body mass index before pregnancy, maternal weight gain during pregnancy) influence birth weight. Furthermore, neonates’ birth weight is associated with socio-economic conditions, especially maternal education level, household income, and living-situation. The better educated women the healthier is their lifestyle and the more likely infants are born normal weight. Therefore, strategies on health education for women of child-bearing age are very important to improve the precondition for healthy children.

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For centuries the island of Okinawa has had a reputation for the longevity of its population. For 30 years after reversion to Japan, from 1970, Okinawa had the longest life expectancy of all prefectures in Japan. However this advantage was lost in 2000 and male longevity is now ranked 26th among the 47 prefectures of Japan, almost 2 years less than Nagano Prefecture. The aim of this study was to explore whether the recent decline in Okinawan life expectancy advantage is due to the cohort effect of low birthweight infants resulting from the starvation following the war, who are now reaching middle age. This is an observational study using existing demographic and health statistics. Reliable data on life expectancy, mortality and low birthweight rates are available since reversion to Japan. The low birthweight rate for Okinawa is 20% greater than the Japanese mainland. In the year 2000 the longevity advantage of Okinawans males over the Japanese mainland was lost and the relative life expectancy of females declined. The mortality ratio for heart disease has reversed, consistent with a cohort effect, with younger Okinawans now having higher death rates than those living in the rest of Japan. The loss of the longevity advantage of Okinawa over the rest of Japan is due to an increase in non-communicable disease and is consistent with the Developmental Origins of Adult disease hypothesis reflecting the post World War cohort of low birthweight infants reaching middle age.

II-34 Coexistence of Anaemia and Obesity among women in North West Morocco
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Rationale & Objectives: Morocco is undergoing nutrition transition marked by the coexistence of nutritional deficiencies and chronic diseases. The aim of this study is to determine the prevalence of anaemia and overweight among women of reproductive age in Kenitra. Materials & Methods: 128 women were recruited when attending vaccination campaign for their preschool children. Anthropometric
parameters and haemoglobin rate were evaluated. Women responded also to a questionnaire on socio-demographic characteristics. Results & Findings: Average age was 28.37 ± 9.1. BMI mean was 25.83 ± 16.5 kg/m2. Mean haemoglobin rate was 11.43 ± 1.5 g/dl. General overweight was reported in 56% and overt obesity (BMI > 30 Kg/m2) in 15.6%. Anaemia prevalence reaches 60%. 51.3% of anaemic women are from rural area while 48.7% are from urban. Only 10.93% of women use iron fortified flour. Conclusion: Nutrition transition expressed by the double burden of anaemia and obesity is pronounced in this area of Morocco. More nutritional education and communication are needed.

**II-35**  
A Survey of Medicinal Plants Used By the Garo Tribal Healers of Netrokona District, Bangladesh  
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The Garo tribe inhabits the north-eastern regions of Bangladesh. They have their own tribal healers and rely on medicinal plant preparations administrated by their healers for treatment of various ailments. It was the objective of the present study to conduct an ethnomedical survey among the Garo tribal healers of Netrokona district. Informed consent was obtained from the healers. Interviews were conducted in the native dialect and medicinal plant samples as pointed out by the healers in guided field-walks were collected and identified at the Bangladesh National Herbarium. The medicinal plant species (with ailments treated given in parenthesis) included Mangifera indica (influenza, helmintiiasis), Syzygium cumini (diabetes), Ziziphus mauritiana (influenza, dysentery), Bambusa vulgaris (urinary tract infections, menstrual irregularities), Musa sapientum (dysentery, wart), Bombax ceiba (urinary calculus, sex stimulant), Psidium guajava (toothache, acne, diabetes), Areca catechu (constipation, helmintiiasis), Borassus flabellifer (debility, insomnia), Cynodon dactylon (wounds), Cardia papaya (dysentery, ring worm), Cocos nucifera (skin diseases, diarrhoea), Colocasia esculenta (to stop bleeding), Averrhoa carambola (diarrhoea, to stop vomiting, influenza), Tamarindus indica (fever, asthma, to stop vomiting), Amorphophallus campanulatus (skin diseases), Lawsonia inermis (eczema, leprosy, jaundice), Emblica officinalis (jaundice, gastric ulcer, indigestion), Crataeva religiosa (gonorrhea, toothache), Citrus grandis (skin diseases), Ficus racemosa (diabetes), Justicia gendarussa (bone fracture, pain), Duranta repens (malarial fever), and Thevetia peruviana (mental disorder). Information on indigenous use of medicinal plants has led to discovery of many medicines in use today. Scientific studies conducted on the above medicinal plants may lead to discovery of more effective drugs than in use at present.

**II-36**  
Epidemiology of anemia among fertile age women in 5 regions of the Republik of Uzbekistan  
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Purpose of the study: to study spread of anemia in 5 regions of the republic among fertile age women. The materials and methods. The place of the residence of women and quantity: in the Republic of Karakalpakstan -209, Fergana region-190, Khorezm region-152, Tashkent region -185, Tashkent city-166. Representative sample was carried out, quantity of participants of the study were 902 non-pregnant women who are 15-49 years old. The Methods of the study - a determination of C-reactive protein (CRP), ferritin in serum (FS), transferrin in serum (TS) was conducted on biochemical analyzer RANDEX (Daytona). The Hemoglobin was defined by the gemoglobinometer HemoQue. The results and discussions. In Karakalpakstan whole anemia frequency formed 49.8%, from them iron deficiency anemia (IDA) was 36.84% and anemia with indefinite etiology (AIE) was 8.14%. In Khorezm anemia was formed as 34.2%, from them IDA formed 22.36%, AIE was 11.84%. In Fergana from 31.05% IDA formed 18.94%, AIE was 12.10%. In Tashkent region anemia frequency formed 37.29%, from it IDA was 23.78%, AIE was 13.51%. The lowest frequency of anemia was in Tashkent city, it was 29.51%, from it IDA formed 18.67%.

**II-37**  
Cause of high incidence of Adiposity in kids from Sarajevo  
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BACKGROUND: The incidence of childhood obesity has increased dramatically, including severe childhood obesity and obesity-related comorbid conditions. Overweight children tend to have more anxiety and poorer social skills than normal-weight children have. METHODS: Body Mass Index (BMI) is a measure of weight adjusted for height used to determine weight categories. These data were used to determine the rates of diagnosis among various subgroups of children seen in the several pediatries offices in Sarajevo. Feasibility study in the primary care setting include time constraints, cost, training, and expertise in the use of these methods. RESULTS: Pediatric obesity is associated with increased risks of concomitant psychological or psychiatric problems, cardiovascular risk factors, chronic inflammation, type 2 diabetes mellitus, and asthma. Higher economic status does not guarantee that children will live in neighborhoods that encourage more activity. The higher prevalence of obesity was present in both boys and girls with constipation compared with the controls. DISCUSSION: Taller and stunted children had higher obesity risk than normal height for age children. Diets of low energy density, which are typically rich in vegetables, fruits, legumes, and minimally processed grain products, allow obese children to consume satisfying portions of food while reducing their energy intake. CONCLUSIONS: Treatment for children who are overweight or obese seems easy, that is, just counsel children and their families to eat less and to exercise more. Parental obesity is a strong risk factor for a child’s obesity persisting into adulthood, especially for young children.
The effect of nutritional early-life programming on adult body composition and appetite regulation

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Introduction: We investigated nutritional early-life programming effects with low protein diet during either pregnancy or lactation when combined with hypercaloric weaning. Lipid distribution and appetite regulation were assessed in adult offspring using magnetic resonance imaging (MRI) and spectroscopy (MRS). Methods: Pregnant C57BL/6 mice were maintained on low protein (8%; LP) or control (20%; C) diets. At birth, offspring were cross-fostered for lactation to mothers being fed the opposite diet: LP/C (LP in utero, C during lactation) and C/LP. We also included a control group (C/C). At 21 days, offspring from all three groups were weaned to either normal fat (3%; NF) or high (12%; HF) diets. Whole body MRI and localised liver 1H MRS was performed on 15wk-old offspring on a 4.7T VVRIS scanner. Manganese-Enhanced MRI (MEMRI) was performed at 9.4T to assess neuronal activity. Blood parameters were assayed for levels of adipokines. Results: C/LP and LP/C offspring showed greater weight gain and caloric intake than C/C and more so when given HF diet (P<0.0001). This was possibly due to increased appetite as indicated by MEMRI-measured neuronal activity (P<0.05). Higher leptin levels were found in LP/C mice than in controls (P<0.05). C/LP mice appear to have reduced internal adipose tissue deposition (P<0.05) and liver lipid content (P<0.01) while LP/C mice did not differ significantly from C/C. Conclusion: We show that early life undernutrition significantly modifies the adult phenotype. Low protein in the early post-natal period causes beneficial changes in lipid deposition and content despite increased appetite.

Peripubertal folic acid intake alters expression of the DNA repair gene BRCA1 and the pluripotency genes Oct-4 and Sox2.

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Folic acid (FA) intake has been shown to alter cancer risk, at least in part by modifying the epigenome. However, the effects of FA intake during critical phases of development on future cancer risk are not known. We investigated whether variations in FA intake in the peripubertal period induce lasting changes in the expression of genes involved in determining cancer risk. Female Wistar rats were fed AIN93G diet containing either 1 mg FA/kg feed or 5 mg FA/kg feed from weaning on postnatal day 28 until day 56. They were then fed AIN93G containing 1mg FA/kg feed until day 84 when tissues were collected. Gene expression (mRNA) was measured by real time RTPCR. Increased FA intake induced the following changes in gene expression. BRCA1 expression was increased in liver (94%, P=0.04) and adipose tissue (63%, P=0.02). Oct-4 expression was decreased in the liver (43%, P=0.009) and adipose tissue (30%, P=0.0001). Sox2 expression was decreased in liver (58%, P=0.0001), but increased in adipose tissue (86%, P<0.0001). These data show that peripubertal FA supplementation induces tissue-specific alterations in the expression of BRCA1, Oct4 and Sox2 genes, which persist beyond the period of feeding the altered diet. While some induced changes may be protective, the opposite changes in Oct4 and Sox2 expression in liver suggest dysregulation of differentiation. Our findings imply that the ability of FA to modify cancer risk extend beyond recent diet and may, in part, reflect intakes during periods of increased growth and plasticity.

Epigenetic modulation of the SOD1 promoter at birth may have a functional role in the body fat distribution of 9 year old children

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The link between metabolic syndrome and oxidative stress is well established and evidence suggests that antioxidant enzymes such as superoxide dismutase 1 (SOD1) might play a protective role. We investigated the relationship between the epigenetic control of SOD1 and childhood body fat distribution as an indicator of future risk of metabolic syndrome. Sequenom MassARRAY was used to measure individual CpG methylation within the SOD1 promoter, previously identified by methyl-DNA Immunoprecipitation and tiled microarray, in umbilical cord DNA from a Southampton birth cohort. The study received appropriate ethical approval and informed consent. Methylation was related to body composition measured by DXA scanning at age 9 years. Of 4 CpGs/CpG groups with methylation levels that met a priori criteria, independent of sex, the methylation of one had a strong inverse correlation with childhood trunk/limb fat ratio (r²=0.38, n=33). To determine whether methylation of this CpG altered protein binding, we performed an electrophoretic mobility shift assay using nuclear extracts from HepG2 cells. Protein binding at this site was blocked by CpG methylation. In silico examination of this DNA region using MatInspector identified 6 potential transcription factor binding sites. These findings of a link between DNA methylation and both transcription factor binding and childhood body fat distribution suggest that the identified CpG within the SOD1 promoter may have functional relevance. Variations in the epigenetic regulation of genes such as SOD1 may be a key causal process underlying the development of metabolic syndrome.
III-4 Excessive body fat deposition and adverse metabolic profile in adult mice is prevented by reducing dietary n-6 polyunsaturated fatty acids during neonatal life. 

Ailhaud et al, Prog Lipid Res, 2006. 45(3); p203-36

III-5 Fetal programming of hepatic transcriptome in response to gestational dietary protein levels in the pig

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In rodent models and in humans the impact of gestation diets on the offspring’s phenotype was shown experimentally and epidemiologically. The underlying programming of fetal development was shown to be associated with an increased risk of degenerative diseases in adulthood, including the metabolic syndrome. Pigs share many similarities in metabolism, physiology, anatomy and genome with humans and therefore provide a good model. According to the hypothesis that the offspring’s transcriptome is persistently regulated, we aim to identify molecular pathways and candidate genes with relevance to the fetal initiation of postnatal growth and development. Therefore German landrace gilts were fed an isocaloric diet containing protein levels of 30% (high protein - HP), 6% (low protein - LP) or 12% (control protein - CP) during pregnancy. Offspring’s liver tissue was collected at 95th day post conceptum (dpc), 1st, 28th and 185th day post natum (dpn) (n = 48/stage) and used to hybridize onto genome-wide GeneChip Porcine Genome Array (Affymetrix). At 1st dpn the highest numbers of regulated genes were found between HP vs. CP (550 up-, 351 down-regulated). Moreover, levels of AMPK-a2 and PGC-1a were up-regulated at p<0.05; q<0.30). Due to the maternal HP diet genes belonging to the OXPHOS and the steroid synthesis pathways as well as the lipid metabolism (7DCHR, GPX4, SMPD1) were down-regulated. Additionally, lowering LA intake during neonatal development resulted in a healthier plasma lipid profile with significantly reduced fasting triglyceride levels, improved insulin sensitivity (HOMA-IR) and lower fasting resistin and leptin levels. In conclusion, reduction of n-6 PUFA intake during infancy and childhood protected against excessive fat accumulation and an adverse metabolic profile in mice subjected to an unbalanced western style diet during adolescence and adulthood. This study has shown that fat quality of neonatal nutrition plays an important role in early development and could thus program adult body composition and metabolic homeostasis. (1) Ailhaud et al, Prog Lipid Res, 2006.45(3); p203-36

III-6 Effects of tiazolidinediones on maternal insulin resistance at late pregnancy and the consequences on the fetal development.

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Insulin resistance (IR) during pregnancy is responsible for some of the adaptations taking place in the mother that allow normal fetal development. We have previously observed that maternal-IR is associated with low-grade inflammation mediated by p38MAPK activation, and that when this maternal-IR is diminished newborns are smaller and their insulin-glucose relationship is altered. To further characterize the origin of maternal-IR at late gestation, and to investigate how an impaired adaptation to such physiological IR impacts on the future development of the neonate, we used a model of reversion of IR, by treating the mothers daily from day 16 to 20 of gestation with a tiazolidinedione (TZD), antidiabetic drugs used in the treatment of type 2 diabetes. Other group of rats was treated with the vehicle (control). At 20d of pregnancy, TZD-mothers have lower levels of plasma triglycerides, higher of adiponectin and higher insulin sensitivity than controls. Furthermore, placenta and visceral adipose tissue (AT) weight less, and phosphorilation of p38MAPK was lower in AT in TZD-treated mothers when compared to control. At 6 months of age, offspring of TZD-mothers have lower body weight, insulinenia and lipemia, and higher insulin sensitivity (QUICKI) than controls. Our results confirm that IR at late pregnancy is a low grade inflammatory condition, mediated by stress-kinase activation, and that reversion of this state by antidiabetics drugs does not impair the glucose/insulin relationships in the offspring when adults. Whether at longer times, glucose homeostasis is impaired in the offspring remains to be investigated.

III-7 Low protein diet during gestation and lactation alters the GABAergic paracrine signaling mechanism between pancreatic beta and alpha cells

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Previously, we demonstrated that low protein diet (LP) during early development predisposes rats to glucose impairment in adulthood. We hypothesize that this effect is related to changes in the GABAergic system as it regulates insulin and glucagon secretion in the pancreas. Pregnant Wistar rats were fed a control (C) or LP diet during gestation and lactation; offspring of both groups were fed with C diet at weaning (d21). Islets were isolated at d21 and d130 and exposed to varying glucose concentrations; insulin secretion was
measured by radioimmunoassay (RIA) and expression of mRNA of glucagon, GAD65 and GABA receptors, GABA-B1, GABA-Aa1, a4, 2, 3, by Real Time-PCR. At d21, LP females and males had reduced insulin secretion compared to controls. At d130, LP males had increased insulin secretion at high glucose concentrations compared to controls and LP females. By Real Time-PCR adult LP males had a significant up-regulation of GAD65 (p<0.05), GABA-Aa1 (p<0.001) and glucagon (p<0.01) and down-regulation of GABA-A3 (p<0.001). GABA-B1, GABA-A2 and GABA-Aa4 mRNA levels were not significantly different between LP and control animals at d130. GABA-A receptors located on pancreatic alpha cells(s) inhibit glucagon secretion. GABA-A3 significant down-regulation in LP males leads to an increase of glucagon production. To compensate, GABA-Aa1 is increased and beta cells may produce more GABA by up-regulating GAD65 (GABA-producing enzyme in beta cells). Therefore, the LP diet in early age alters the paracrine alpha and beta cell regulation through the GABA-ergic system in the LP males at d130.

### III-8 Allergen induced cytokine release in human placentae - a possible role in fetal programming of allergies?

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Background: Previous animal experiments indicated the transmissibility of general allergic diathesis from the mother to the fetus. All major cell types known to be involved in allergic processes, including dendritic cells, T cells, B cells and mast cells are present in the decidua. Thus, allergen induced mediator release may prime the fetus for easier sensitization in later life. Objectives: To analyse differences in cytokine production from placental tissue of atopic and healthy mothers after contact with a relevant allergen. Methods: We developed a one sided placenta perfusion model with an internal standard to perfuse two separate cotyledons from the same placenta simultaneously with apple allergen-containing medium (mal d 1) and allergen-free medium for 5 hours. Hence, each control cotyledon provides the respective baseline values for quantitative analysis of allergen induced mediator release. Outflow samples were collected and analyzed for immune mediator release. Histamine concentration was determined spectrophotofluorometrically after extraction and derivatization with o-phthalaldehyde. The cytokines IL-2, IL-4, IL-6, IL-10, TNF-alpha and IFN-gamma were analyzed by using a cytometric multiplex bead array. Results: After application of relevant allergens in perfusion medium, a significant time-dependent release of TNF-alpha and IL-6 was detectable in placentae of mothers suffering apple allergy compared to those from healthy mothers. The expression of the other interleukins and histamine was not remarkably altered. Conclusion: Allergens can induce allergy related effects, which may disturb the immunological balance at the feto-maternal interface and might prime the developing fetal immune system for facilitated later susceptibility for allergic sensitizations.

### III-9 Postnatal growth rate and gestation length are independently related to cardiac autonomic function in lambs

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Background: Small size at birth is associated with adult cardiovascular risk, possibly secondary to preterm birth, reduced fetal growth or accelerated postnatal growth. Markers of cardiovascular risk in adults include heart rate (HR) and heart rate variability (HRV), both indices of cardiac autonomic function. We hypothesised that (a) preterm birth and (b) growth promotion with nutritional supplements, would independently affect cardiac autonomic activity. Objective: To examine the effects of gestation, birth weight, nutritional supplementation and postnatal growth on HR and HRV in lambs. Methods: Singleton ewes were randomised to term (n=23; 1460.2 d) or preterm (n=17; 1370.3 d) delivery. Lambs received nutritional supplements or water, in addition to suckling, from d3-14. ECGs at 4 months of age were analysed to yield HR and HRV derivatives LFnu (reflecting cardiac sympathetic activity) and LF/HF (reflecting cardiac sympatho-vagal tone). Data were analysed using ANOVA and multiple linear regression. Results: Nutritional supplementation did not increase early growth rate (d1-14) or influence HR or HRV. Preterm lambs had increased HR (1208 bpm vs 1055 bpm, p=0.03), LFnu (557 vs 384, p=0.006) and LF/HF (3.407 vs 20.4, p=0.002). Indices of autonomic activity increased with decreasing gestation across the gestational age range (136-151d) [HR (2.3bpm/d, p=0.04), LFnu (3.46/d, p=0.0003) and LF/HF (0.29/d, p=0.002)] and with increasing early postnatal growth rate [LFnu (1.5/g-1 k-1d-1, p=0.008) and LF/HF (0.16/g-1 k-1d-1, p=0.04)]. Conclusions: Reduced gestation length and increased postnatal growth rate are associated with increased cardiac sympathetic activity, possibly contributing to the link between size at birth and cardiovascular disease.

### III-10 Effect of maternal fat-rich diet on cardiac function in adult rat offspring

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Maternal diet-induced obesity in rats is reported to affect offspring cardiovascular system including altered sympathetic control, endothelial dysfunction and vascular abnormalities. However, effect of maternal fat-feeding on cardiac function in offspring has not been directly assessed. Sprague-Dawley female rats were fed either a control (4% fat, n=6) or lard-enriched (24% fat, n=6) diet for 10 days prior to mating, and throughout pregnancy and lactation. There was no increase of maternal weight or plasma leptin concentration following short-term fat-feeding versus controls. No effect of maternal diet on basal cardiac contractility in 9-month-old offspring were observed as tested by left ventricle developed pressure (LVDP), heart rate (HR) and coronary flow (CF) on a Langendorff-perfused isolated heart. In both male and female progeny, there were no differences in LVDP or left ventricle end diastolic pressure (LVEDP) after global ischemia (20-min) and reperfusion between offspring of fat-fed dams (OF) and controls (OC). However, post-ischemic recovery of CF was affected by maternal diet with more pronounced drop in OF males during reperfusion (p=0.05). Similarly, recovery of both HR and CF were more affected in OF then in OC females after ischemia-reperfusion (HR:p=0.01;CF:p=0.05). Myocardial infarct size was similar between OF and OC. In conclusion, fat-feeding in the absence of maternal
obesity in pregnant rats, did not alter the cardiac contractile function, is associated with declined coronary function in response to ischemia-reperfusion, independently of gender. These data may provide important insights into the long-term cardiovascular consequences of maternal fat-feeding per se in pregnancy and during suckling.

### III-11 Effects of Accelerated Growth on Modulation of Body Fat Distribution and Hypothalamic Activation in Mice

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**Introduction:** Epidemiological studies have revealed a relationship between accelerated growth and a high risk of chronic development of obesity. Here we assessed the effect of accelerated growth on body fat distribution and hypothalamic nuclei in male mice born small and large. Methods: At birth, C57BL/6 male mice were identified as small or large (according to length/weight). At age 3 weeks they were weaned onto a normal fat diet (3% fat) during 12 weeks. Whole body and liver 1H MRS were performed at the end of the experiment on a 4.7T Varian system. Neuronal activation was assessed by manganese-enhanced MRI (MEMRI) on a 9.4T scanner on the fed state. Results: Large mice gained more weight during the first 10 days of lactation than small mice (3.62±g vs. 3.32±g; p<0.01). This effect was reversed after weaning (small=16.5±3.3g vs. large=14.7±3.2g; p<0.001). Caloric consumption relative to body size increased in small mice after 6 weeks of feeding compared to large mice (46.4±2 kcal/g vs. 42.1±9 kcal/g; p<0.001). No significant differences in body adiposity or liver fat content were observed between the groups. Energy efficiency (body weight gain/Kcal intake) was increased in small mice compared to large mice during the first 6 weeks. MEMRI-measured neuronal activity in the paraventricular nucleus showed significant increase in signal intensity in small mice compared to large male mice. Conclusion: Small size at birth and accelerated growth after weaning influenced region-specific brain activity associated with appetite and satiety, which reflected behavioural modification through increased caloric intake.

### III-12 Influence of Neonatal overfeeding in rats on obesity and tissue-specific regulation of glucocorticoid converting enzymes during development

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**BACKGROUND:** Clinical and experimental evidence shows that a hyperactivity of glucocorticoid metabolism was postulated to be involved in the early life programming of the metabolic syndrome in adulthood. **OBJECTIVE:** To determine the effects of postnatal overfeeding on obesity and glucocorticoid-activating enzyme 11 hydroxysteroid dehydrogenase type 1 (11-HSD1) and glucocorticoid-inactivating enzyme 5α-reductase 1 (5αR1) during development.**METHODS:** The effects of neonatal overfeeding in rats, obtained by reducing the size of the litter in the immediate postnatal period and then given standard chow after weaning. 11HSD1 and 5αR1 mRNA level in adipose tissue or/and liver were measured at 3w, 4w, 5w, 6w, 8w and 16w of age. **RESULTS:** Neonatal overfeeding induces early-onset adiposity and adult obesity with insulin resistance. 11HSD1 mRNA level in retroperitoneal adipose tissue (RAT) but not in epididymal adipose tissue (EAT) were significantly increased with postnatal day and peaked at 6 weeks in both control and overfeeding. After then, 11-HSD-1 mRNA levels in RAT was significant higher in overfeeding compared with control. 5αR1 mRNA level in liver were decreased with postnatal day in overfeeding but not in control,while 11HSD1 mRNA level in liver were higher in overfeeding compared to control at all sampling age. **CONCLUSIONS:** The findings demonstrate a long-term effect of neonatal overfeeding that can program major changes in the development of glucocorticoid-converting enzymes and metabolic alterations in adulthood.

### III-13 Exogenous leptin treatment in naïve neonatal rats permanently influences sympathetic control of blood pressure in later life

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**OBJECTIVE:** Leptin plays an important role in the sympathetic activation of the kidney, implicated in obesity-related hypertension. We have recently reported increased blood pressure in young offspring of obese rats; associated with enhanced sympathetic tone. In order to investigate whether the exaggerated leptin surge plays an aetiological role in the development of hypertension in this model, exogenous leptin was administered to control pups; using a regimen designed to mimic the exaggerated leptin surge in the neonates of obese dams. Methods Recombinant rat leptin (L, 3g/kg, PeproTech, UK) or saline (S) was injected at postnatal day 9-14. At day 30, blood pressure was recorded using mouse radio-telemetry probes (DSIPhysioTel PA-C10) and cardiovascular response to restraint stress was determined. Heart rate variability (HRV) was derived from the telemetry record by autoregressive spectral analysis. Results Leptin treated rats (L) demonstrated increased systolic blood pressure compared to controls (S) (SBP [mmHg, mean±SEM] male L, 131±6.2 versus S, 119±4.3, n=6, P<0.05; female L, 129±7.4 versus S, 115±3.8, n=6, P<0.05) with exaggerated cardiovascular responses to restraint stress (P<0.05). Low/High frequency ratio of HRV, indicative of sympathetic tone, was significantly increased in leptin- versus saline treated mice (P<0.01). Heart weight was increased in leptin-versus saline treated animals (P<0.01). Conclusions Early onset hypertension in offspring of obese rats is associated with evidence for increased sympathetic tone and enhanced sensitivity to leptin. This study implicates a central role for neonatal leptin in the origins of hypertension observed. Hyperleptinaemia during critical periods of hypothalamic plasticity results in enhanced sympatho-activation and hypertension.
III-14 Maternal high fat diet during pregnancy and lactation alters maternal care and independently alters offspring development

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Background: Altered maternal nutrition and care independently increase susceptibility to disease. We therefore hypothesized that an interaction may exist between a maternal high fat (HF) diet and maternal care, subsequently impacting on offspring phenotype. Methods: Wistar rats were mated and randomized to: control dams fed a control diet (CON) or dams fed a HF diet from conception until the end of lactation (HF). Maternal care was assessed by observing maternal licking and grooming of pups between postnatal day (P)3-P8. Postweaning, offspring were fed a control (-con) or HF (-hf) diet, resulting in CON-con, CON-hf, HF-con, and HF-hf groups. From P27, pubertal onset was assessed. At ~P105 estrus cyclicity was investigated. Results: Maternal HF diet reduced birth weight (p<0.001) and reduced maternal care; HF-fed mothers licked and groomed pups less than CON dams (p=0.01). At P27, retroperitoneal fat:body weight ratio was greater in pups from HF-fed dams compared to CON (p=0.0001). Pups from HF-fed dams went into puberty early and this effect was exacerbated by a postweaning hf-diet (p=0.05). Maternal HF and postnatal hf diets independently altered estrus cyclicity in females; 58% of HF-hf offspring exhibited prolonged estrus; 22% in HF-con, 38% in CON-hf and 11% on CON-con groups. All postnatal effects were independent of maternal care. Conclusions: Maternal HF diet during pregnancy and lactation altered maternal care and led to increased pre-pubertal adiposity, early puberty and altered estrus cyclicity. A postweaning hf-diet exacerbated this phenotype. Maternal nutritional signals, independent of maternal care, alter offspring body fat and reproductive function.

III-15 Erratic eating promotes weight gain and may decrease insulin sensitivity in juvenile lambs

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Background: Obesity and type 2 diabetes are increasing health problems in lower socioeconomic groups where food supply is often uncertain. We investigated the effects of erratic eating pattern on weight gain and metabolism in juvenile lambs. Methods: Prepubertal, female lambs were housed in group pens and randomly assigned to receive, for 6 weeks, maintenance feed given twice daily in equal portions (C; n=16), or the same weekly feed amount given in aliquots of variable size at unpredictable times (E; n=17). Insulin sensitivity was assessed pre and post intervention by intravenous glucose tolerance test (IVGTT) and insulin tolerance test (ITT) [n = 6 (C) and 7 (E) lambs in abstract; data on all animals will be presented]. Areas under the curve (AUC) were calculated. Data were compared using t tests. Results: Total feed intake per animal was similar (C 86.0kg, E 85.7kg). Weekly %weight gain was initially reduced in E lambs (week 1: -6.00.2 vs 1.00.1; p=0.064) but greater in E lambs thereafter, significant at week 5 (8.00.2 vs 2.00.1%; p=0.01). In all lambs, from before the intervention to after, fasting plasma glucose concentration decreased (3.50.1 vs 3.10.1mmol.l-1, p<0.0001) and IVGTT AUC increased (77351 vs 90636 mmol.l-1.min, p=0.05). Change in ITT glucose AUC was negative in E lambs, suggesting reduced insulin sensitivity post intervention (C 1116, E -5 7), but this was not statistically significant (p>0.05). Conclusions: Erratic eating increases weight gain, even when caloric intake is not increased, and may be associated with insulin resistance in juvenile lambs.

III-16 The Liver X-Receptor (LXR) gene promoter is hypermethylated in a mouse model of prenatal protein restriction

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Prenatal nutrition has been epidemiologically identified as a determinant of adult disease. Feeding low-protein diets during pregnancy in rodents is a well-established model to induce 'programming' events in offspring. One proposed underlying mechanism for fetal programming is altered DNA methylation. We hypothesized that protein restriction would induce epigenetic adaptations that would interfere with lipid metabolism and hence predispose to atherosclerosis. Methods: C57BL/6 mice were fed protein restricted diet during pregnancy. Cpg island methylation microarrays were performed on fetal liver DNA on day 19.5 of pregnancy. Results: 204 gene promoter regions were found to be differentially methylated upon protein restriction. Hypermethylation and hypomethylation were found in comparable numbers. The liver receptor (Lxr) alpha promoter was hypermethylated in protein-restricted pups. Lxr alpha is a nuclear receptor critically involved in control of cholesterol and fatty acid metabolism. The mRNA level of Lxrα was reduced by 32% in fetal liver upon maternal protein restriction. Expression of the Lxr target genes Abcg5/Abcg8 was reduced by 56% and 51%. In vitro methylation of a mouse Lxrα-promoter/luciferase expression cassette resulted in a 24-fold transcriptional Lxrα repression. Conclusions: Our study demonstrates that, in mice, protein restriction during pregnancy interferes with DNA methylation in fetal liver. As hypermethylated and hypomethylated regions are comparable in numbers, it is unlikely that only a shortage of methyl groups by protein restriction is the underlying cause. Lxrα was identified as a new target of differential methylation. We speculate that changes in DNA methylation contribute to the relationship between early nutrition and adult disease.

III-17 Protein restriction during gestation affects DNA methylation patterns at several gene promoters in rat hypothalamus.

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Protein restriction during embryonic and fetal development induces an intra-uterine growth restriction (IUGR) and increases the susceptibility to develop metabolic disorders later in life. This early life nutritional programming affects tissue growth, organization and metabolism via molecular mechanisms that are still poorly known. Epigenetic regulation of gene expression is known to suffer from nutritional alterations and may be responsible for observed long term effects. We have shown that protein restriction during gestation (8% versus 20% protein in the maternal diet) affects the hypothalamic expression of several genes involved in the control of foetal growth, energy balance, central metabolism and food intake (hypothalamic neuropeptides -NPY, AgRP, CART, POMC-, receptors -LEPR, NPY2R, MC4R-, signal transducers -SOCS3-). Among them, are also included several imprinted genes which regulation is closely related to epigenetic mechanisms (GRB10, H19, Gnas, SNRPN). Slight modifications in the DNA methylation patterns of several promoter regions were identified in response to IUGR. We are now studying on our model the influence of the level
III-18 Exogenous leptin treatment in naïve neonatal rats permanently induce leptin resistance, hyperphagia, and obesity
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Objective: Leptin plays a critical role in energy homeostasis through inhibition of appetite. We have recently reported hyperleptinemia and increased adiposity in the adult offspring of obese rats. In order to investigate whether the exaggerated leptin surge plays an aetiological role in the development of leptin resistance in this model, we administered diet to control pups; using a regimen designed to mimic the exaggerated leptin surge in the neonates of obese dams. Methods: Recombinant rat leptin (L, 3g/kg, PeproTech, UK) or saline (S) was injected at postnatal day 9-14. At day 30, anorexic responses to leptin challenge was assessed in fasted animals using leptin (10mg/kg). Organ weights were recorded and serum stored at -80°C. Food intakes were measured weekly. Results: At 30 days of age, body weight was similar between the two groups, although female L showed a greater inguinal fat mass than S (P<0.05). At 60 days of age, L rats weighed more than S rats (body weight [g] male L, 238.2 ± 12.1 versus S, 222.9 ± 9.6; female L, 196.9 ± 6.5 versus S, 188.5 ± 10.9, n=0.5, n=6) and had markedly greater inguinal fat mass (P<0.01). Leptin treated rats (L) developed leptin resistance at 30 days of age (P<0.05) and hyperleptinemia from 6 weeks of age. Conclusions: L-L demonstrates an apparent leptin resistance with reduced inhibitory actions of leptin on food intake. We hypothesise that neonatal hyperleptinemia leads to a permanent impairment in leptin-signalling and a consequent reduction in leptin’s neurotrophic effects. Such effects may underlie the subsequent development of hyperleptinemia and increased adiposity.

III-19 Exposure to cadmium during pregnancy induces gender-specific epigenetic regulation and expression of glucocorticoid receptor (GR) in liver of neonates
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Prenatal exposure to cadmium (Cd2+) induces a mild but significant lower birth weight (BW) associated to increased levels of foetal circulating glucocorticoids (GC). Both, low BW and exposure to GC have been associated to altered epigenetic regulation and are ‘hallmarks’ of developmental programming. Objective: to study the effect of prenatal exposure to Cd2+ in the methylation status of the GR promoter in liver of male and female neonates and to assess whether this pattern of methylation is associated to GR expression (mRNA and protein). Methods: virgin female Wistar rats were mated and then treated with 50 ppm of Cd2+ (as CdCl2 in drinking water) during pregnancy. GR methylation status was determined in bisulphite-treated DNA of females and males neonate’s livers. The GR methylation assay covered 30 CG dinucleotides in promoter region ranging from -2536 to -2361. The methylation status of each locus was analysed individually by pyrosequencing. GR expression was assessed by real time PCR and GR protein was determined by WB. Results: liver of exposed males showed a total hypermethylated status (185% related to control) in the 9 CpG sites contained in the promoter of GR which was associated to a lower expression (mRNA and protein) of the GR. On the contrary, in exposed females, WB. Results: liver of exposed males showed a total hypermethylated status (185% related to control) in the 9 CpG sites contained in the promoter of GR which was associated to a lower expression (mRNA and protein) of the GR. On the contrary, in exposed females, GR was hypomethylated (62%) and its expression was increased. Conclusion: prenatal exposure to Cd2+ induces a gender-specific epigenetic regulation of liver GR in neonates determining GR expression. This effect may be associated to the development of sex-related pathologies at adult age. Support: Fondecyt # 1071110.

III-20 Hepatic proteome profile of neonatal piglets born to gilts fed diets with different protein levels during pregnancy.
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We determined the effect of the maternal dietary protein level during gestation on the hepatic porcine proteome. Fifty eight gilts (age 241 ± 4 days, body weight 150.6 ± 10.5 kg) were randomly assigned to three dietary groups with different dietary protein levels obtained from 87 piglets with high (> 1.46 kg) and low birth weight (< 1.1 kg) born to gilts fed throughout gestation: adequate protein (AP, 12% CP), high protein (HP, 30% CP) and low protein (LP, 6% CP). Liver samples of methyl donors and cofactors in the maternal diet on the methylation status of DNA in offspring suffering an IUGR induced by a protein restriction during gestation. Two weeks before conception and during gestation and lactation, rat females are fed four different diets containing either 8 or 20% protein and a low or high amount of methyl donors and cofactors (methionine, choline, Vit B12, zinc, betaine). The first results on this animal model will be presented.

III-21 Postnatal nutritional supplements affect growth and appetite in lambs
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Background: Nutritional supplements containing protein and carbohydrate are used in small babies to promote growth. The effects of altered dietary composition in the postnatal period on appetite, growth, and metabolism are not known. Methods: Term-born lambs
were allowed to suckle freely from their mothers and were randomised to receive an oral supplement from 3-14 days of age containing protein, carbohydrate and vitamins designed to increase caloric intake by 25%, or to controls. Twins were randomised as pairs. Milk intake was measured in single lambs between one and two weeks using D2O dilution. All lambs underwent intravenous glucose tolerance test (IVGTT) at 4 months of age. Groups were compared using ANOVA. Results: In singletons, supplemented lambs had slower growth velocity in the first 2 weeks of life (Supplemented n=20, 421 g.kg⁻¹.day⁻¹ vs Control n=22, 461 g.kg⁻¹.day⁻¹, p=0.004) and milk intake tended to be decreased (1818 vs 2058 ml.kg⁻¹.day⁻¹, p=0.06). However in supplemented twins, growth velocity tended to be faster (Supplemented n=10, 422 g.kg⁻¹.day⁻¹, p=0.06) and milk intake was similar (1897 vs 1878 ml.kg⁻¹.day⁻¹). After four months, single lambs had greater baseline plasma glucose concentrations than twins, (3.90 ± 3.60 mmol.l⁻¹), and greater glucose AUC (8533 ± 6326 mmol.l⁻¹.min) and insulin AUC (1258 ± 7714 mg.ml⁻¹.min) (all p=0.05) but there was no effect of supplements on IVGTT. Conclusion: Nutritional supplements may promote postnatal growth where nutrition is marginal, but altered dietary composition may also suppress appetite and adversely affect early growth. The balance of macronutrients in the postnatal diet may be important in appetite regulation.

III-24 Elucidating the Genomic and Epigenomic Mechanisms of Nutritionally Regulated Developmental Programming

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Mechanisms by which specific developmental challenges, such as nutritional insults resulting from maternal undernutrition, can lead to fetal programming remain unknown. We characterized the impact of undernutrition in utero on global changes in gene expression in liver, rhomboidaeus, diaphragm, soleus, and heart. Ingenuity pathway analysis revealed a striking dysregulation of a metabolic pathway centering on FBXO32 and FOXO3a. Expression of FBXO32, a muscle atrophy inducing protein, increased significantly in all tissues (from 2 to 20-fold). FOXO3a, a transcriptional regulator of FBXO32 with roles in myogenesis and metabolism, had significant upregulation in all tissues except for the liver. Furthermore, several known imprinted genes showed differential expression in the SGA piglets. Preliminary data indicates that increased expression of IGf2 appears to be the result of hypermethylation within IGF2/H19 differentially methylated regions (DMRs). We hypothesize that muscle atrophy occurs in SGA through increased Foxo3a expression to provide energy needed for the development of essential organs. We are currently investigating the extent to which gene expression is regulated in this model of SGA via methylation of CpG islands within promoter regions of target genes.
III-25 Insulin sensitivity in 18 month old offspring born to ewes undernourished 60d before to 30d after conception.  
Mark Oliver, Anne Jaquiery, Sarah Todd, Frank Bloomfield, Jane Harding  
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Background: Maternal undernutrition during pregnancy may increase the risk of diabetes and obesity in offspring. We have previously shown that adult offsprings of ewes undernourished around the time of conception had impaired glucose tolerance. We investigated whether this was due to impaired insulin sensitivity. Methods: Ewes were undernourished from 60d before to 30d after mating (PCUN) or well fed (N). Offspring underwent hyperinsulinaemic-euglycaemic clamps at 18mth of age (PCUN: 10 single, 10 twin, 7 male, 13 female; N: 6 single, 20 twin, 12 male, 14 female). Insulin sensitivity of glucose (ISGlu) was calculated as the steady-state (SS) glucose infusion rate divided by SS plasma insulin concentration. Data were analysed by multiple regression. Results: PCUN did not affect birth weight (N: 5.47±0.1; PCUN: 5.47±0.2kg) or weight at 18mth (N:81±72; PCUN: 77±72kg). Males were heavier at 18mth (86±7 vs. 74±1kg, p<0.001). Twinning had no effect on birth weight or weight at 18mth. Basal or SS plasma glucose and insulin were not affected by sex, twinning or PCUN. ISGlu was not affected by sex, birth weight, twinning or PCUN (N: 1271; PCUN: 1272 mg.mL.microunits-1.kg-1.min-1). Increasing weight at 18mth reduced ISGlu (-0.3 mg.mL.microunits-1.kg-1.min-1/kg, 95%CI:-0.6, -0.1, p<0.01). Conclusions: Impaired glucose tolerance in young adult offspring of PCUN ewes is not secondary to reduced insulin sensitivity. It is, therefore, likely secondary to impaired insulin secretion in response to a glucose load, particularly during the first phase. The mechanisms underlying this insulin secretory defect remain to be determined.

III-26 Foetal protein-malnutrition of the F1-generation in mink (Neovison vison) causes changes in F2 progeny  
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Protein malnutrition during foetal life can induce metabolic changes in offspring. An adequate protein provision during pregnancy might therefore be of particular importance for a strict carnivore species e.g. mink and cat, due to their high requirement for dietary protein. Indeed, the mink, due to its spontaneous insulin resistance, may prove to be a useful animal model in studies of obesity and type-2-diabetes. Our objectives were to investigate if changes detected in foetal hepatic tissue of the F1-generation caused by low protein provision during foetal life can be transmitted to the F2-generation. Further, to study postnatal growth of the F2-generation. Traits studied included reproductive performance, energy and protein metabolism, key hepatic enzymes associated with glucose homeostasis, metabolic hormones and kit growth. The F0 generation were fed either a low-protein (14% of metabolizable energy (ME) from protein - FLP1) or an adequate-protein (29% of ME from protein - FAP1) diet for the last 17?9 days 3?6 days of gestation. The F1 dams were studied at birth and at one year of age after maintenance on an adequate diet from birth and onwards. Metabolic traits during gestation and lactation were mainly unaffected by protein supply during foetal life, but F2 offspring of FLP1 dams had significantly higher birth weight than those of FAP1 dams. Furthermore, the relative abundance of pyruvate kinase mRNA was significantly higher in male FLP1 than FAP1 females (P=0.05). Food intake did not differ across males, however, HF and HP females consumed more HFHS diet than C (P<0.01). Total AUC for GIP was higher in HF than HP (P=0.009). HF males had higher fasting ghrelin than HP and C (p<0.01) with a trend in HF males (p=0.1). Total AUC for GIP was higher in HF than HP (p=0.009). HF males had higher fasting GIP than HP and C males (p=0.01). While maternal HP and HF diets have minimal lasting effect in male offspring, female offspring of HF are protected against and HP offspring predisposed to greater weight gain and body fat in adulthood.

III-27 Sex Differences in Offspring Body Weight and Food Intake after Prebiotic Fiber or High Protein Maternal Diet  
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The negative effects of malnourishment in utero have been widely explored, but effects of increased maternal macronutrient intake are not known in relation to high fiber, and have been inconclusive with regards to high protein. Virgin Wistar dams were fed either a control (C), high protein (40% wt/wt) (HP) or high prebiotic fiber (25% wt/wt) (HF) diet throughout pregnancy and lactation. Male and female pups consumed C diet from 21d to 100d of age and were then switched to a high fat/sucrose (HFHS) diet for 8 wk. A DEXA scan and oral glucose tolerance test were performed. Blood was analyzed for ghrelin, GIP, amylin, insulin, leptin and PYY. Mass and body fat (%) in males did not differ between groups, but were lower in HF versus HP females (p<0.01). Food intake did not differ across males, however, HF and HP females consumed more HFHS diet than C (p=0.05). There was a significant sex effect for fasting and total AUC for ghrelin and fasting GIP, with females having higher levels than males (p<0.02). HF females had higher fasting ghrelin than HP and C (p<0.01) with a trend in HF males (p=0.1). Total AUC for GIP was higher in HF than HP (p=0.009). HF males had higher fasting GIP than HP and C males (p=0.01). While maternal HP and HF diets have minimal lasting effect in male offspring, female offspring of HF are protected against and HP offspring predisposed to greater weight gain and body fat in adulthood.

III-28 Dietary fat quality during development affects body fat accumulation in adult mice  
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We previously reported that dietary fat quality of postnatal nutrition, i.e. fatty acid composition, plays an important role in the development of body composition in mice (Oosting et al. 2009). The current study investigates whether another aspect of dietary fat quality in postnatal nutrition, i.e. the physical properties of fat globules, may also affect development of body composition. The production process of infant milk formula (IMF) alters the physical properties of the fat globules compared to raw milk (RM; Lee et al., 2002). We developed an IMF with a complex lipid matrix (CLM) which more closely resembles the physical properties of fat globules in RM, and we evaluated the long term effects of CLM versus standard IMF (CTR) on body composition in mice. Postnatally, between 16 and 42 days of age, male C57Bl/6j mice were subjected to a diet containing either CLM or CTR. Subsequently, a moderate Western style diet (WSD, 10 w%f) was fed until dissection at 126 days of age. Body composition was monitored by dual x-ray absorptiometry at 42, 70, 98 and 126 days of age. Although body weight was not affected, fat accumulation was reduced and lean body mass was increased in adult mice raised on CLM diet compared to CTR diet. Hence, exposure to a diet early in life with a RM-like fat quality prevented excessive fat accumulation when challenged with a moderate WSD during adulthood.
II-29  Milk lacking a-casein leads to permanent reduction in body size in mice

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The major physiological function of milk is the transport of amino acids, carbohydrates, lipids and minerals to mammalian offspring. Caseins are the major milk proteins and are secreted in the form of a micelle consisting of protein and calcium phosphate. We have analysed the role of a-casein for lactation by inactivating the corresponding gene in mice. The absence of a-casein protein significantly curtails secretion of the other casein proteins suggesting a role for a-casein in the establishment of the casein micelles. The reduction in casein micelle secretion is accompanied by a ten-fold drop in the concentrations of milk calcium and phosphate. Secretion of whey proteins and transcription of the other casein genes are also reduced, while secretion of albumin, which is not synthesized in the mammary epithelium, into milk is not reduced. Despite these deficiencies offspring nursed by a-casein deficient dams survive. However, their growth during lactation is severely delayed. Cross-fostering reveals that this impairment is not dependent on pup genotype. After weaning growth-impaired pups show some compensatory growth but do not reach the weight of control mice nursed by wild-type dams throughout life. Despite the growth deficiency, the general development of pups is only delayed transiently, and for a number of physical and behavioural development parameters no difference was found between pups nursed by a-casein deficient females and control pups. These results demonstrate that a-casein deficiency in mice has a significant effect on milk protein composition, milk protein secretion and life-long body size of the offspring.

II-30  Maternal dietary restriction during early pregnancy affects the expression of enzymes involved in hepatic lipid and glucose metabolism in the pups.

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We have previously shown, that undernutrition in the mother at early pregnancy, promotes hepatic lipid deposition, and accelerates the age-related insulin resistance in the adult offspring in a sex specific manner. To further characterize these alterations, we hypothesized that intrauterine malnutrition may affect the expression of enzymes involved in liver metabolism in the perinatal period. To test this hypothesis, from mating until 12d of pregnancy, one group of rats was fed ad libitum (control) whereas another group was allowed to eat 60% the amount fed by controls (underfed). From this time on, all animals were fed ad libitum. Expression of enzymes involved in lipid and glucose metabolism were measured in fetuses (20 day) and in newborns (1 day). When compared to controls, newborns of underfed dams had lower body weight. In the transition from intrauterine to extrauterine life, there was a decrease in the expression of acetylCoA carboxylase and FA synthase, whereas no difference was found in the newborns of underfed mothers. After delivery, the induction of the expression of the enzymes regulating gluconeogenesis (PEPCK, glucose 6-phosphatase), was lower in neonates born from underfed than from controls. When compared to controls, the expression of CPT1, pyruvate dehydrogenase and the transcription factor (CEBP-alfa) was lower in pups born from underfed mothers. In conclusion, malnutrition during early pregnancy compromises normal foetal growth and alters the mRNA expression of enzymes involved in the regular metabolic adaptations to extrauterine life, that may have long term consequences in the offspring when adults.

II-31  Poor maternal nutrition leads to alterations in oxidative stress, antioxidant defense capacity and markers of fibrosis in rat islets - Potential underlying mechanisms for development of the diabetic phenotype in later life.

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Poor early nutrition in humans and animals increases future risk of developing type 2 diabetes (T2D). There is good evidence that the environment plays an important role in this relationship, however, the mechanisms underlying this association are poorly defined. Oxidative-stress is instrumental in T2D pathogenesis and islets are particularly susceptible to oxidative-stress, due to reduced antioxidant defence. Islet fibrosis is an important contributor to T2D. Here we use our maternal low protein rat model to determine the effect of early diet on oxidative-stress and fibrosis in pancreatic islets at 3 and 15-months of age. Gene expression by RT-PCR in 3 and 15-month control and LP male rat pancreatic islets revealed significantly (p<0.05) increased expression of xanthine oxidase in 15-month LP offspring, suggesting increased oxidative-stress. Copper-zinc superoxide dismutase (CuZnSOD), (p<0.05), manganese superoxide-dismutase (MnSOD), (p<0.01) and heme oxygenase-1 (HO-1), (p<0.01) antioxidant enzyme expression were significantly reduced in LP offspring, indicating impairment of oxidative defence. Significantly increased expression of fibrosis molecules collagen I (p<0.01) and collagen III (p<0.05) was also observed in 15-month LP offspring. Angiotensin-II-receptor-type-I (ATII-R1), induced by hyperglycaemia and oxidative-stress, was significantly (p<0.05) up-regulated in 15-month LP offspring. Lipid-peroxidation, measured by ELISA, was significantly (p<0.05) increased in 15-month LP animals. LP offspring also developed age-associated hyperglycaemia. We conclude that maternal protein-restriction causes age-associated increased oxidative-stress, impairment of oxidative defence and fibrosis in pancreatic islets. These findings provide potential mechanisms by which suboptimal early nutrition can lead to T2D development later in life.

II-32  Immediate and long term effects of a neonatal diet enriched in proteins on growth and adipose tissue development

Ousseny Sarr, Florence Gondret, Agnès Jamin, Isabelle Le Huërou-Luron, Isabelle Louveau

The high protein content of formula offered to babies born with small weights is suspected to increase the risk of later obesity. This study examines the immediate and long term effects of neonatal diets differing in protein content on growth and adipose tissue features of pigs born with small birth weights. Piglets (10th percentile) were fed milk-replacers formulated to mimic sow milk (AP: 4.4 g of protein/100 kcal) or provide an excess of proteins (HP: 6.2 g of protein/100 kcal) from day 2 to weaning (day 28). Ten piglets were
killed at day 28. Others piglets (n = 25) were then offered ad libitum a high fat diet (12% fat) up to day 160. From birth to weaning, HP piglets had a greater daily weight gain (P < 0.05). Relative weight of perirenal adipose tissue, mean adipocyte diameters and specific activities of lipogenic enzymes in perirenal and subcutaneous adipose tissues were lower (P < 0.05) in HP than in AP piglets at this age. Thereafter, growth performance did not differ between dietary groups. At day 160, percent body fat did not differ between HP and AP pigs. However, there was a trend towards greater proportion of enlarged adipocytes in perirenal and subcutaneous adipose tissues of HP pigs. Moreover, basal rates of glucose incorporation into adipocytes were lower in HP than in AP pigs. In summary, our data clearly show that a high protein formula induced a temporary reduction in adipose tissue development and altered adipose tissue physiology in the long-term.

III-33 Metabolomics and Proteomics responses to perinatal protein restriction in intra-uterin growth restricted (IUGR) rats with or without catch-up growth.

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Too small size at birth has been associated with higher risks of developing metabolic syndrome in adulthood. However, the underlying mechanisms of such ‘foetal events’ or ‘programming’ are largely unknown. This study was conducted with an intra-uterine growth restriction (IUGR) rat offspring model by using proteomic and metabolomic approaches to investigate the hypothesis that energy balance could be deregulated by IUGR and that early or late ‘catch-up growth’ could modulate this deregulation, particularly in hypothalamic centres involved in feeding behaviour. We have analysed by LC-MS the plasmatic metabolic responses of the male offspring from pregnant rats fed with control diet or protein restricted diet during gestation only or during gestation and lactation. We used two-dimensional gel electrophoresis combined to MALDI-TOF to identify hypothalamic proteins. These high throughput approaches showed a clear discrimination between the perinatal nutritional groups and allowed detection of subtle plasmatic and hypothalamic changes in IUGR offspring. In particular, maternal protein restriction seems to be associated with deregulation of key proteins implicated in glycolysis and fatty acid beta-oxidation, in glutamate production or in growth cone guidance. Decrease of several amino acids (tryptophan, leucine, methionine, arginine,...) and an increase of carnitine metabolites are associated with protein restricted status. The identification of the metabolites which contribute to this discrimination is still in progress. Further functional study on the dynamic change proteins and metabolites may lead to better understanding the mechanisms of IUGR and its modulation according to early or late ‘catch-up growth’.

III-34 Maternal DHA supplementation reduces fat mass in the neonate guinea pig

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We investigated the effects of maternal docosahexaenoic acid (DHA) supplementation on body weight and fat mass development in the neonate guinea pig. Female guinea pigs were fed a diet supplemented or not with 0.75% DHASCO oil (corresponding to 2.4% DHA of total fatty acids) during pregnancy and lactation. After 21 days of age, the pups from both groups were fed a chow diet, until the end of the experiment (d105). The fatty acid analysis of the dam’s milk, collected 3 days after delivery, showed detectable levels of DHA (1.8% of total fatty acids) only in the supplemented group. At 2 days of age, the body weight of pups was identical in both groups while the % of fat mass was lower in the DHA supplemented group. At d21, this difference in % fat mass between groups was attenuated but still significant. Between d21 and d63, when the offspring were fed a chow diet, a catch up fat mass was observed in the +DHA group. At d105, no difference in either body weight or body composition was observed between the groups. These results indicate that perinatal DHA intake reduces fat accretion during fetal life and/or the first postnatal days. This effect is followed by a compensatory catch up fat after discontinuation of DHA intake. Further studies will be needed for understanding the mechanism of action of DHA on adipose tissue development in early life and the consequences later on.

III-35 Effect of a high protein diet on food intake and liver metabolism during pregnancy, lactation and after weaning in mice

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Major hepatic metabolic pathways are involved in the control of food intake but how dietary proteins affect global metabolism to adjust food intake is incompletely understood, particularly under physiological challenging conditions such as lactation. In order to identify these molecular events, mice were fed a high protein (HP) diet from pregnancy, during lactation until after weaning and compared to control fed counterparts. Liver specimens were analyzed for regulated proteins using 2-D gel electrophoresis and MALDI-TOF-MS and plasma samples for amino acids, glucose and urea. Based on 26 differentially expressed protein spots associated with an exhausted liver glycogen content, elevated urea and citrulline plasma concentrations we conclude that HP feeding during lactation leads to an activated amino acid, carbohydrate and fatty acid catabolism while it activates gluconeogenesis. From pregnancy to lactation, plasma arginine, tryptophan, serine and glutamine decreased while urea concentrations increased in both feeding groups. Concomitantly, hepatic glycogen content decreased while total fat content remained unaltered in both groups. Consideration of 59 proteins differentially expressed between pregnancy and lactation highlights different strategies of HP and control fed mice to meet energy requirements for lactation by adjusting urea cycle, amino acid degradation, carbohydrate and fat metabolism, citrate cycle, but also ATP turnover, protein folding, secretion of proteins and (de)activation of transcription factors. In conclusion, the identification of differentially expressed proteins may help to explain HP feeding and lactation induced changes of hepatic metabolism but also offers novel candidates potentially involved in the adjustment of food intake and thus for energy homeostasis.
Altered nutrition during the F0 pregnancy changes the phenotype of F1 and F2 pregnant rats
Samuel Hoile, Nicola Thomas, Karen Lillycrop, Mark Hanson, Graham Burdge
University of Southampton, SOUTHAMPTON, UNITED KINGDOM

There is evidence for the transmission of altered phenotypes between generations in several taxa. The mechanism underlying such transmission between generations is not known. We investigated in rats the effect of feeding an altered diet during F0 pregnancy on physiological outcomes and hepatic gene expression in F1 and F2 dams. Wistar rats were fed diets with 25% more energy with either sufficient (PS) (18% (w/w)) or restricted (PR) (9% (w/w)) protein contents during pregnancy. Dietary energy content was maintained throughout the life course in F1 and F2 generations. Dams were killed on post-conceptional (PC) day 8.5 or allowed to deliver naturally. Pregnancy weight gain was lower (40g) in F1 and F2 dams (PC age*generation P<0.0001) irrespective of F0 protein intake. There was no difference in energy intake, litter size, length of gestation or litter weight. Plasma glucose was significantly lower and -hydroxybutyrate higher in F2 compared to F0 dams (generation both P<0.0001). Corticosterone concentration was increased in F1 and F2 dams contingent on F0 protein intake (generation* F0 diet P=0.023). On PC day 8.5, F0 diet and generation altered hepatic glucocorticoid receptor, phosphoenolpyruvate carboxykinase and phosphofructokinase-2 mRNA expression (interaction all P<0.0001). The results suggest that altered nutrition during pregnancy induced changes in maternal physiology and gene transcription in subsequent generations. This suggests that an altered intra-uterine environment represents one mechanism for the transmission of induced phenotypes between generations. Furthermore, sustained environmental change may induce adaptation over the course of several generations.

Late gestation undernutrition (LG-UN) affects overall development and thyroid function in sheep
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Objective: To assess 1) whether LG-UN have long-term implications for development of different organ systems, and 2) whether the postnatal diet affects the phenotypical expression of foetal programming. Methods: Twenty twinpregnant ewes were fed a NORM (energy and protein) or LOW (50% of NORM) diet the last 6 wks of gestation (term=147d). Twin lambs were from age 3d-6mo assigned to each their feeding: CONV (moderate) or HCHF (High-Fat-High-Carbohydrate). Male lambs were slaughtered at 6mo (~puberty). Female off-spring were raised on pasture from 6mo-2yrs (young adulthood) and then slaughtered. Results: Growth until 6 mo of age was determined exclusively by the postnatal diet. LG-UN resulted in smaller adult body size with most tissues/organs being proportionately smaller, but thyroid and adrenals were increased in LOW animals. HCHF lambs at 6mo had massive fat infiltration in adipose tissue; functional hepatocyte mass and kidney weight was reduced. By 2yrs (after 1 yrs on a moderate diet), postnatal diet effects disappeared, except for redistribution towards higher abdominal:renal fat in HCHF compared to CONV animals. Postnatal nutrition determined serum T3 and T4 in young lambs being highest in HCHF lambs, but in adult animals prenatal nutrition effects became manifested (highest in LOW). Conclusions: We have demonstrated implications of LG-UN for thyroid development and regulatory function, possibly involved in earlier termination of growth and smaller adult body size in LG-UN individuals. LG-UN effects were rarely detectable in adolescent lambs, where the actual postnatal diet was the main determinant. LG-UN effects, however, became consistently manifested in early adulthood.

A maternal low protein diet programs glucose and fatty acid metabolism differentially in adult male and female mouse offspring
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Nutritional conditions during human fetal life can influence the risk to develop the metabolic syndrome in adult life (metabolic programming’). Dysregulated fatty acid metabolism and impaired glucose tolerance are hallmarks of the metabolic syndrome. We aimed to establish a mouse model of metabolic programming focusing on the effects of a maternal low protein diet during gestation on glucose and lipid metabolism in the adult offspring. Methods: Pregnant C57BL/6J mice received a control or a low protein diet throughout gestation. Offspring received a low postnatal diet or a high fat diet from 6-22 weeks of age. Glucose metabolism was studied with a whole-body-glucose test using [6,6-2H]-glucose. Hepatic gene expression was characterized by microarray. Results: Maternal low-protein-diet did not affect glucose metabolism in male offspring. Male offspring showed lower insulin sensitivity after receiving a high fat diet than female offspring, regardless of the diet of the dam. Female offspring from normal-protein fed dams was relatively resistant to diet-induced metabolic dysregulation. Maternal low-protein-diet during gestation led to deteriorated insulin sensitivity upon high-fat feeding in female offspring. Conclusions: We conclude that, in mice, maternal protein restriction during gestation does not change the glucose response to a high fat diet in male offspring. However, gestational protein restriction changes fatty acid and glucose metabolism in female offspring in such a way that it resembles male metabolism. Our study shows limited effects of fetal malnutrition in male mouse offspring. On the contrary, females presented a masculinized reaction to a high-fat challenge when derived from a protein-restricted dam.

Early origins of disease: mild maternal zinc deficiency during pregnancy causes obesity and insulin resistance in the offspring
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Zinc is critical for insulin function; however, interactions between Zn, insulin, and glucose metabolism are complex. Mild maternal Zn deficiency affects maternal carbohydrate metabolism and fetal growth, but mechanisms behind changes in offspring glucose homeostasis are not understood. Rats were fed Zn deficient (ZnD, 7g/g) or control diet (CON, 25 g/g) for 3 weeks, bred and kept on ZnD during pregnancy and lactation. Litters were culled to 7pups/dam. After weaning, pups were fed regular chow. Insulin and glucose tolerance tests were performed at 5 and 10 weeks of age. Rats were killed at 3 and 15 weeks of age. mRNA expression of adipokines
Coordinated changes in expression of imprinted and craniofacial genes resulting from TWSG1 deficiency suggest transcriptional co-loss of TWSG1, producing a normal phenotype. Importantly, this group of genes also showed marked enrichment for imprinted genes. Among them were several craniofacial genes (Eya4, Lhx8, Prrx2, Satb2, Tbx22), the upregulation of which could compensate for the downregulation of genes that showed opposing expression changes with upregulation in unaffected mutants but downregulation in affected mutants. With phenotypic severity. Remarkably, unaffected mutants also differed transcriptionally from wild type embryos. We identified a group of genes that were upregulated in Twsg1-/- embryos at E10.5 (classified as severely affected, moderately affected or unaffected). Transcriptional alterations correlated with maternal status at conception. Control or Fe and Zn deficient rats were supplemented with Fe, Zn, Fe+Zn or placebo throughout pregnancy. At weaning, body weight (BW), Fe status, liver hepcidin and intestine Fe transporter expression were determined. Effects of Fe and Zn supplementation on offspring reflected maternal status at conception. Zn supplementation with or without Fe decreased BW if dams were not deficient at conception whereas Fe supplementation increased BW. Zn supplementation of dams not deficient at conception did not affect Fe status but liver Fe and hepcidin expression were significantly higher. However, Zn supplementation of deficient dams decreased hepcidin expression in their offspring. Fe and Fe+Zn supplementation was associated with lower ferroportin levels in dams not deficient at conception. In conclusion, while Zn supplementation during pregnancy does not affect Fe status of the offspring, Zn supplementation of mothers with adequate Fe and Zn status increases liver Fe and compromises offspring BW. Therefore, potential adverse effects of Zn supplementation should be evaluated.

Pregnant women world-wide are frequently Fe and Zn deficient. Therefore, co-supplementation with Fe and Zn during pregnancy is common. While Fe supplementation programs are successful, studies suggest that Zn supplementation negatively impacts maternal Fe metabolism. However, little is known about effects of maternal Fe or Zn supplementation on Fe metabolism in the offspring. We developed a rat model to investigate if Fe and/or Zn supplementation during pregnancy affects regulation of Fe absorption and Fe status in their offspring and if these effects are dependent upon maternal Fe and Zn status at conception. Control or Fe and Zn deficient rats were supplemented with Fe, Zn, Fe+Zn or placebo throughout pregnancy. At weaning, body weight (BW), Fe status, liver hepcidin and intestine Fe transporter expression were determined. Effects of Fe and Zn supplementation on offspring reflected maternal status at conception. Zn supplementation with or without Fe decreased BW if dams were not deficient at conception whereas Fe supplementation increased BW. Zn supplementation of dams not deficient at conception did not affect Fe status but liver Fe and hepcidin expression were significantly higher. However, Zn supplementation of deficient dams decreased hepcidin expression in their offspring. Fe and Fe+Zn supplementation was associated with lower ferroportin levels in dams not deficient at conception. In conclusion, while Zn supplementation during pregnancy does not affect Fe status of the offspring, Zn supplementation of mothers with adequate Fe and Zn status increases liver Fe and compromises offspring BW. Therefore, potential adverse effects of Zn supplementation should be evaluated.

Severity of craniofacial birth defects may vary widely even when the underlying mutation is the same. The sources of this variation are poorly understood. Influence of the environment and epigenetic phenomena are increasingly recognized as major mechanisms of this variability in humans and mice. Mice deficient in Twisted gastrulation (TWSG1), a modulator of bone morphogenetic proteins, serve as a model to study these phenomena. Twsg1-/- newborns have a spectrum of craniofacial defects in an inbred C57BL/6 background that vary with phenotypic severity. Remarkably, unaffected mutants also differed transcriptionally from wild type embryos. We identified a group of genes that showed opposing expression changes with upregulation in unaffected mutants but downregulation in affected mutants. Among them were several craniofacial genes (Eya4, Lhx8, Prrx2, Satb2, Tbx22), the upregulation of which could compensate for the loss of TWSG1, producing a normal phenotype. Importantly, this group of genes also showed marked enrichment for imprinted genes. Coordinated changes in expression of imprinted and craniofacial genes resulting from TWSG1 deficiency suggest transcriptional co-regulation and/or alterations of epigenetic states, such as methylation. It remains to be determined how maternal diet during pregnancy, either methyl-rich or methyl-donor-deficient, would affect the frequency and severity of craniofacial defects in Twsg1-/- embryos.

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The concept of metabolic programming supports the idea that nutritional and hormonal status during key periods of development, impacts, first, hypothalamic neuronal organization and then determine the long term control of energy balance by programming future feeding behaviour and energy expenditure. We therefore examined the consequence of early or late ‘catch-up growth’ after intrauterine growth restriction of rat male offsprings, on multiple molecular and cellular events taking place in the developing hypothalamus and searched for correlation, at adulthood, on feeding behaviour and energy expenditure. We therefore examined the consequence of early or late ‘catch-up growth’ after intrauterine growth restriction of rat male offsprings, on multiple molecular and cellular events taking place in the developing hypothalamus and searched for correlation, at adulthood, on feeding behaviour and energy expenditure. We therefore examined the consequence of early or late ‘catch-up growth’ after intrauterine growth restriction of rat male offsprings, on multiple molecular and cellular events taking place in the developing hypothalamus and searched for correlation, at adulthood, on feeding behaviour and energy expenditure. We therefore examined the consequence of early or late ‘catch-up growth’ after intrauterine growth restriction of rat male offsprings, on multiple molecular and cellular events taking place in the developing hypothalamus and searched for correlation, at adulthood, on feeding behaviour and energy expenditure. We therefore examined the consequence of early or late ‘catch-up growth’ after intrauterine growth restriction of rat male offsprings, on multiple molecular and cellular events taking place in the developing hypothalamus and searched for correlation, at adulthood, on feeding behaviour and energy expenditure.
III-43 The effect of maternal undernutrition during the first 90 days of gestation on neonatal lamb behaviour and survival

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This study investigated whether maternal undernutrition in early gestation had differential effects on the behaviour and survival of neonatal lambs in two genotypes of sheep: a breed adapted to harsh environments (Scottish Blackface: BF) and a breed selected for rapid lean tissue growth (Suffolk: S). Control ewes (C: BF=41, S=38) were fed 100% of requirements for maintenance and foetal growth whereas Restricted ewes (R: BF=45, S=44) were fed 0.75 of requirements between days 1 and 91 of pregnancy over 2 years. Data on neonatal lamb behavioural progress to standing and sucking for the 267 lambs born were collected from videotape. Lamb reactivity was recorded at handling at 30 minutes old (year 1 only). There was an interaction of breed and treatment on lamb birth weight as SR lambs, but not BFR lambs, were lighter than their C counterparts (P=0.004). BF lambs were quicker to stand and suck than S lambs (P<0.001) and there was a trend towards SR lambs taking longer to achieve each behavioural milestone. R lambs took longer to suck from their mothers than C lambs (P=0.08), and were more likely to need assistance to suck (P=0.09). BFR lambs were more reactive than other groups to the handling tests (P=0.009) and more vocal than BFC lambs (P=0.026). In year 1, but not year 2, R lambs had higher mortality than C lambs (P=0.02). These data suggest that undernutrition in early gestation affects early behavioural development in the neonate, and that these effects are differentially influenced by breed.

III-44 Physiological significance of stimulation by the intake of protein-to-digest to cholecystokinin secretion during the suckling period for the development of pancreatic digestive functions in piglets

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Objective: Most protein matter in breast milk consists of large molecule protein which infants need to digest. We, thus, evaluated the physiological significance of stimulation by the intake of protein-to-digest to cholecystokinin secretion during the suckling period for the development of pancreatic digestive functions, using a piglet model. Methods: Piglets were artificially reared on a standard piglet formula with milk protein or a piglet formula with milk protein hydrolysate (molecular weight: <3,500) from 7 to 21 days of age. Pancreas weights, pancreatic digestive enzymes and plasma cholecystokinin concentrations were measured at 21 days of age. We also examined if a hydrolysate formula can sufficiently stimulate cholecystokinin secretion using dam-fed piglets at 19 days of age. Results: Pancreas weights and pancreatic digestive enzymes in hydrolysate formula-fed piglets were significantly less than those in standard formula-fed piglets at 21 days of age. In contrast, pancreatic insulin concentration in hydrolysate formula-fed piglets was significantly higher than that in standard formula-fed piglets at 21 days of age. The basal level of cholecystokinin in the plasma at 21 days of age was significantly low in hydrolysate formula-fed piglets, compared with standard formula-fed piglets. At 19 days of age, significant increase in plasma cholecystokinin concentration by oral administration of the hydrolysate formula was not observed, whereas the standard formula raised plasma cholecystokinin concentration. Conclusions: Our recent results suggest that the stimulation by dietary protein during the suckling period may be necessary for the proper development of pancreatic digestive functions.

III-45 Altered nutrition during the F0 pregnancy in rats changes the phenotype of F1, F2 and F3 female offspring

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Exposure during F0 pregnancy alone to different diets changes phenotypic changes in the offspring which can be transmitted between generations. There is little information about the transgenerational effects of persistent environmental change on the offspring’s phenotype. We investigated the effect of increasing dietary energy over three generations on the phenotype of the adult female offspring. Wistar rats were fed diets with 25% more energy compared to the breeding colony diet from F0 conception until the third generation. Protein intake during F0, but not F1 or F2 pregnancy, differed by 50%. In each generation, females were either mated at day 70, or killed and tissues collected. Weight gain was less in offspring of F0 protein-restricted (PR) females in all generations (P<0.05), while energy intake was significantly greater in F2 offspring irrespective of F0 protein intake (P<0.05). Proportional liver weight was greater in F3 than F2 and F1 offspring (generation P<0.0001). Plasma glucose was lower in F3 PR line offspring than F1 offspring (generation and F0 diet, P<0.0001). Leptin was lower in F2 and F3 and corticosterone higher in F3 offspring than F1 offspring (generation P<0.0001). Glucagon and -hydroxybutyrate concentrations were unchanged. These findings show that increased F0 energy intake induced changes in offspring physiology between generations which for some outcomes were contingent on F0 protein intake. Thus specific aspects of the phenotype follow different patterns of change to an initial challenge between generations despite subsequent environmental stability. Such processes may have utility in adaptation of species to novel environments.

III-46 Effects of a maternal high protein diet during pregnancy and/or lactation on offspring development, and lactation in mice

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Consequences of increased protein intake during pregnancy and lactation on offspring are not well defined. We have previously shown in rats that a maternal high protein diet causes reduced birth mass and energy metabolism and hypothesized that exposure to maternal excess protein intake disturbs offspring long-term development. Mouse dams were fed a high (HP, 40%) or a control protein (C, 20%) diet from mating to weaning (21d). After birth standardized litters were cross-fostered to different dams fed C or HP which resulted in three groups (C-C, C-HP, and HP-C) representing diet exposure during pregnancy and lactation. Litters were weaned on a standard rodent diet. Body mass development, body fat accretion, blood metabolites, and locomotive activity were studied in male offspring.
from birth to 1 year of age. Additionally, maternal milk and mammary gland (MG) parenchyma were analysed. Dams fed HP diet during pregnancy gained less body mass (-25-56%), and showed 13% lighter litters and a reduced litter size (10 vs. 11, P<0.05). MG parenchyma was reduced by 10-12% and milk lactose % of dams fed HP during pregnancy was lower (1.6 vs. 2.0%). Offspring body mass was reduced in the C-HP group, however, body fat accretion and locomotive activity did not differ between groups. No changes in plasma metabolites were observed. Our study demonstrates immediate negative effects of HP diet fed during pregnancy and lactation on maternal body mass, rearing performance, and lactation. However, growth of the HP offspring was only transiently affected during adolescence.

III-47 The Influence of birth weight on hepatic adiponectin receptor 2 (AdipoR2) and fatty acid synthase (FAS) in neonatal pigs
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Birth weight (BW) can determine later health, including the development of metabolic syndrome. Adiponectin regulates lipid metabolism and glucose homeostasis; its receptor, AdipoR2, is abundantly expressed in the liver. FAS catalyses lipid biosynthesis and both FAS and AdipoR2 are regulated hormonally and nutritionally. This study examined whether BW influences AdipoR2 and FAS gene expression in liver of neonatal pigs. Piglets from eleven litters were ranked according to BW and three animals from each litter were assigned to small (S), normal (N) or large (L) groups. Animals were humanely euthanased on 7 (n=15) or 14 (n=18) days of age and tissue sampled. Gene expression was quantified by real-time PCR. Plasma metabolites and leptin were also analysed. On day 7, L pigs had higher gene expression of FAS than N pigs (L, 2.40.4; N 1.00.2 fold change (p<0.05)). On day 14, N pigs had higher gene expression of AdipoR2 than S pigs (S, 2.20.1; N 2.90.3 fold change (p<0.05)). AdipoR2 and FAS were positively correlated with plasma leptin on day 7 in the L group only (P<0.05). Despite the rate of lipid biosynthesis being low in neonatal pigs, due to the high fat content of milk, L pigs exhibited raised hepatic FAS expression, suggesting an increased capacity for lipid biosynthesis. The reduction in AdipoR2 in S piglets suggests a reduced adiponectin signalling capacity and thus an increased potential for insulin insensitivity.

III-48 The short term effects of maternal overnutrition during gestation and lactation on hepatic steatosis, adiposity and metabolic abnormalities in rat offspring
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Inadequate maternal diet has been linked to offspring metabolic diseases. This study was designed to develop a rat model to investigate the development of hepatic fat accumulation, adiposity and metabolic abnormalities in offspring from dams fed a diet rich in fat and carbohydrates during gestation and lactation. In this model, the combined effect of maternal overnutrition and litter size reduction on the development of metabolic traits in the offspring was further investigated. Pregnant Spraque-Dawley rats were either offered a chow diet plus chocolate or a chow diet only during gestation and lactation. At birth, offspring were randomly cross-fostered within the diet groups into small and normal litters with four and ten offspring per litter. After weaning, offspring were kept on the same diet as their mothers throughout the entire experimental period. The maternal diet high in chocolate resulted in increased birth weight, blood glucose as well as liver TG and glycogen content in offspring until 1 week of age. At 3 weeks of age increased adiposity, as well as increased plasma and liver TG were seen in high fat fed offspring. From 3 until 12 weeks of age the chocolate diet resulted in increased liver glycogen in females and plasma TG in males. Increased adiposity and liver TG concentration were also seen at 12 weeks of age in high fat fed offspring. In conclusion, a maternal gestational and postnatal diet rich in fat/carbohydrates affects the metabolic function of the offspring and could thus potentially predispose for development of metabolic diseases.

III-49 Adaption of rabbit preimplantation blastocysts to maternal type 1 diabetes
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We have investigated the effects of short- and long-term hyperglycaemia in 6 days old rabbit preimplantation blastocysts. The blastocysts were grown in diabetic mothers or cultured in vitro. In female rabbits type 1 diabetes was experimentally induced by alloxan treatment 10 days before mating. Short time adaption of blastocysts to different glucose concentrations (1; 10 and 25mM) was investigated by in vitro culture for 1 to 4 hours. Type 1 diabetes led to retardation in blastocyst development, an increase of apoptotic cells in the embryonic disc and a decrease in expression of the antiapoptotic gene bcl-x(L). The insulin receptor (IR) and IGF1 receptor were downregulated in both models, in vivo and in vitro, demonstrating a loss of insulin growth factor sensitivity of the embryo. The glycogenic enzyme hexokinase was upregulated in vitro and downregulated in diabetic blastocysts while the gluconeogenic enzyme PEPCK was decreased in in vivo and in vitro grown blastocysts. Our results document that embryonic (i) glucose metabolism and (ii) IR/IGF-signalling are strongly affected by hyperglycaemia. The dramatic loss of growth factor sensitivity results in a dysregulation of early embryonic development. Shifts in the IR/IGF1R system are a potential risk factor for negative consequences in embryonic metabolic programming processes. Supported by the German Research Council (DFG; NA 418/4-2).

III-50 The impact of protein quality of early diet on later glucose homeostasis in intra uterine growth restricted (IUGR) rats
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Background - IUGR, resulting in low birth weight, increases the risk of later development of metabolic diseases including diabetes. The impact of protein quality of early diet on later susceptibility to diabetes development in at risk population is not known. Aim -
The long-term impact of protein source of early diet (casein and whey), on later glucose homeostasis was investigated in IUGR rats. Methods - IUGR was induced in SD rats by 50% food restriction during last 10 days of gestation and resulted in a 15% reduced birth weight of offspring. Two groups of the IUGR pups (n=20/group) were fed ad-libitum an AIN93 based-diet with either 20% casein (CAS) or 20% whey (WHEY) from 3 to 6 weeks of age. All animals were then fed a chow diet until 28 weeks of age. Intra-peritoneal glucose tolerance test (IPGTT) was performed at age of 6 and 27 weeks. Results - At age of 6 weeks, CAS relative to WHEY had significantly lower basal glucose and showed reduced glucose peak and area under curve (AUC) with higher insulin AUC in response to IPGTT. Furthermore CAS relative to WHEY had also long term benefit in view of significantly lower basal insulin and higher HOMA insulin sensitivity later in life (age of 27 weeks) (P<0.05, in all cases). Conclusion - Results highlight the influence of the source of protein early in life on glucose homeostasis in the short-term and reveal, for the first time, its long-term impact on insulin sensitivity later in life for a population at risk of diabetes.

III-51 Changes in Maternal Dietary Fatty Acid Composition During Pregnancy and Lactation Alter Vascular Function of Adult Offspring
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Human populations exhibit temporal and cross-sectional variations in fatty acid intake. Variations in dietary saturated (SFA) polyunsaturated (PUFA) and trans fatty acid (TFA) intakes alter cardiovascular disease (CVD) risk in adults. Little is known about the effect of fatty acid exposure during development on future cardiovascular function. To investigate this, female rats were fed either 7% (w/w) soybean oil (SO, low n-6:n-3 PUFA), hydrogenated soybean oil (HSO, TFA), butter (SFA), fish oil (FO, eicosapentaenoic and docosahexaenoic acid enriched) or safflower oil (SAO, high n-6:n-3 PUFA) from 2 weeks prior to mating until offspring were weaned. Offspring were weaned onto AIN93M (4% soybean oil). Blood pressure and ex-vivo resistance artery endothelial function were measured in 77 day old offspring. Maternal diet significantly altered (P<0.0001) systolic (SP) and diastolic (DP) pressure in the offspring contingent on sex (interaction P < 0.01). In males, SP and DP differed by maternal diet; HSO > SO, butter = FO = SAO. In females, SP and DP were HSO = SO, butter = FO > SAO. Maternal diet significantly (P<0.01) altered endothelial-dependent arterial relaxation pEC50 and maximum relaxation contingent on sex (interaction P < 0.01). These data show that even at adequate total intakes, changes in the fatty acid composition of the maternal diet induce persistent changes in the vascular function of the offspring. If applicable in humans, such findings have important implications for dietary persistence changes to pregnant women to reduce their children’s future CVD risk.

III-52 Conjugated linoleic acid incorporation in rats plasma after feeding an enriched diet during early life
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Previous studies demonstrated that the intake of 1% Conjugated Linoleic Acid (CLA) diet during early infancy in an 80:20 mixture of cis 9,trans-11 and trans-10,cis-12 exerts some effects on their immune system, mainly on immunoglobulin production. To determine whether immune effects are correlated with CLA incorporation in plasma after feeding CLA; and whether CLA incorporation modifies plasma fatty acid profile. Dietary supplementation was performed during suckling and/or early infancy. After the dietary intervention, fatty acid composition and c9,t11 and t10,c12 CLA isomers content were quantified in 4-wk-old rats plasma by fast gas chromatography. CLA isomers were detected in plasma of all CLA-supplemented animals, and the highest content was quantified in rats supplemented during the longest period (p<0.05). Plasma from reference rats had no content of t10,c12-CLA, which were lower than those found in the rest of the groups. The relative proportion between c9,t11 and t10,c12 CLA was higher in all CLA supplemented groups (90-10) than that of the original mixture (80:20). Feeding CLA resulted in several changes in the fatty acid profile of plasma. The proportion of the major n-6 fatty acid, linoleic acid (C18:2), was significantly reduced in all CLA supplemented groups (p<0.05). Furthermore, the relative content of C22:5 and C22:6 was significantly increased in animals CLA fed (p<0.05). In overall, the CLA mixture fed was efficiently incorporated in plasma of 28 day-old animals and consequently modified the fatty acid profile. Thus, CLA plasma incorporation is correlated to the immune effects described after CLA diets.

III-53 Complex changes in hepatic fatty acid composition and gene expression of newborn mice in response to a mild supplementation of maternal diet by n-3 long-chain polyunsaturated fatty acids
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Postnatal development is affected by long-chain omega-3 polyunsaturated fatty acids (n-3 LC-PUFA) transported into foetus from maternal circulation and ingested by newborns with milk during lactation. Aim of this work was to characterize the effects of a very mild n-3 LC-PUFA supplementation (5% of dietary fat replaced by EPA/DHA concentrate; EPAX 1050 TG; EPAX AS, Aalesund Norway) of mothers’ diet (6% wt/wt total fat content) on: (i) the fatty acid composition of lipids in milk, liver and plasma of the offspring at 10 days and 30 days after birth; and (ii) body weight, food intake and liver gene expression at 10 days. The n-3 LC-PUFA intake had no effect on body weight and milk consumption. Milk EPA concentration was marginally elevated, while DHA concentration increased 10-fold. Complex fatty acid composition analysis revealed differences in total lipid spectra in milk, plasma and liver in every analyzed time point, which was associated with changes in the liver gene expression of the pups. Results suggest significant effect of the relatively mild supplementation of mothers’ diet by n-3 LC-PUFA on liver functions of the newborns.
III-54  Maternal diabetes compromises hypothalamic neural development and induces leptin resistance in the offspring of mice.
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Maternal diabetes is a common complication of pregnancy and offsprings of mothers with diabetes have a much great risk to develop obesity and type II diabetes later in life. Despite these observations, the biological processes mediating the disturbance in metabolic programming and energy balance regulation are not well understood. In the present study, we explored the consequences of maternal diabetes on the development of hypothalamic neural circuits involved with the regulation of energy balance. To this aim, we used a mouse model of maternal hypoinsulinemia induced by streptozotocin (STZ) injections that leads to persistent hyperglycemia. The results indicate that induction of diabetes during gestation is associated with changes in the offsprings’ growth as revealed by a significant increase in body weight curves in the pups of STZ-treated dams as compared with control mice. Mice born to diabetic dams also have increased fasting glucose and increased food intake during adult life. These impairments in metabolic regulation were associated with leptin resistance during adulthood. Furthermore, the ability of leptin to activate intracellular signaling in arcuate neurons and the density of neural projections from the arcuate nucleus to the paraventricular nucleus of the hypothalamus were significantly reduced in pups born to diabetic dams. Together, these data show that hypoinsulinemia during gestation has long-term consequences on energy metabolism. They also indicate that animals born to diabetic dams display abnormal organization of hypothalamic feeding pathways that may be the result of diminished responsiveness of hypothalamic neurons to the trophic actions of leptin during neonatal development.

III-55  Methyl deficient diets modify the fatty acid composition of phosphatidyl choline in the fetal brain.
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There is increasing evidence that methyl deficient diets, i.e. low in folic acid, choline and methionine, adversely affect fetal development. Measurements of methyl flux have shown that the maternal liver is a major site of methyl metabolism in the pregnant rat and that the principal product is phosphatidyl choline (PC), used for the export of fats from the liver. Lipid export is reduced when the diet is deficient in choline, leading to changes in lipid metabolism in both dam and fetus. To evaluate the effects of deficiencies on the fatty acid composition of the fetal brain, pregnant rats were fed one of two experimental diets; either one deficient in folic acid, or one deficient in all three key methyl donors, folic acid, choline and methionine. Animals were killed on d21 of gestation. Total fats were extracted and phospholipids separated by chromatography. Total levels of choline, phosphocholine, phosphatidylcholine (PC), and phosphatidyl ethanolamine (PE) were unchanged in the fetal brain of rats fed methyl deficient diets. Choline deficient diets increased the proportion of C18, C20:4n6 and C22:4n6 fatty acids in PC extracted from the fetal brain. This result suggests that the de novo synthesis of PC from PE is increased when the mother is fed a low choline diet and that this changes the fatty acid composition of PC in the fetal brain. The close interrelationship between methyl deficient diet and fat metabolism suggests that the choline supply should be considered in interventions aimed at altering the PUFA composition of the fetal brain.

III-56  Stress During Lactation Affects Fatty Acid Amide Hydrolase Expression but not Type 1 Cannabinoid/Endocannabinoid Receptors in Adult Mice
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Stress during lactation induces metabolic disturbances and overweight in adult mice. These metabolic alterations may be reversed with a type 1 cannabinoid/endocannabinoid receptor (CB1ER) antagonist, suggesting hyperactivity of these receptors in metabolic disruptions due to early stress. Hyperactive CB1ER may be a direct consequence of its elevated expression, or indirectly by decreased fatty acid amide hydrolase activity (FAAH; the enzyme able to inactivate endocannabinoid agonists). Objective: To evaluate the effects of a nociceptive stress (NS) during lactation on adult liver (L) and epididymal fat (EF) CB1ER expression, and FAAH expression and activity. Methods: Twelve hours old, male mice pups were randomly distributed for maternal cross-fostering. During lactation, mice were stressed or not with a daily subcutaneous injection of saline solution in the back. Adult mice were sacrificed and EF and L extracted to evaluate mRNA expression of CB1ER and FAAH by RT-PCR. Protein expression was performed by Western blot. Additionally, EF and L-FAAH activity was determined by its ability to hydrolyze 3H-[Anandamide] at 37°C. Results: Our NS model lead to increased body weight, EF and triglycerides levels in adult mice. During lactation, mice were stressed or not with a daily subcutaneous injection of saline solution in the back. Adult mice were sacrificed and EF and L extracted to evaluate mRNA expression of CB1ER and FAAH by RT-PCR. Protein expression was performed by Western blot. Additionally, EF and L-FAAH activity was determined by its ability to hydrolyze 3H-[Anandamide] at 37°C. Results: Our NS model lead to increased body weight, EF and triglycerides levels in adult mice. Messenger RNA expressions of CB1ER, FAAH together with CB1ER protein did not change. Interestingly, FAAH protein and enzymatic activity decreased by 40-50% in NS-mice. Conclusions: Stress during lactation decreases protein expression and activity of adult EF and L-FAAH, leading to sustained availability of endocannabinoids in both tissues. As a result, hyperactive CB1ER may be part of a concerted mechanism by which triglycerides accumulate in adipose tissue. Supported by FONDECYT-CHILE 1070663.

III-57  Satiety hormone response to the prebiotic fiber, oligofructose, differs in rats raised in small versus large litters.
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The objective of this study was to examine weight gain and satiety hormone profiles of rats raised in small or large litters from birth to 3 wk of age and then weaned onto control or oligofructose (OFS)-enriched diets. Small litters (SL, n=3/litter) and large litters (LL, n=12/litter) of male Sprague-Dawley rats were randomized to 1 of 4 diets at age 21d: 1) Normal Energy density (NE), 2) NE + 10% OFS, 3) High Energy density (HE), 4) HE + 10 % OFS for 16 wk. DEXA and an oral glucose tolerance test were performed. Plasma satiety hormones and glucose were measured. At weaning, SL body weight was higher (p<0.05) than LL. At 19 wk, OFS tended to reduce body weight to a greater extent in SL than LL but was not significant. Body fat (%) in LL rats decreased on NE+OFS compared to NE whereas no difference was observed for SL rats. Total AUC for GLP-1 was higher (p<0.02) for LL rats on HE than NE; SL rats responded similarly but to a lesser extent. LL rats had greater reductions in total AUC for GIP, insulin and leptin on OFS versus control
compared to SL rats. Overall high fiber feeding showed favourable effects for SL and LL rats. Satiety hormone response to the oral glucose load was blunted in SL rats suggesting potential metabolic disturbance compared to LL rats. As hypothesized, diets enriched with fiber were able to mitigate some but not all of the increased susceptibility to obesity in later life.

III-58  Body fat accumulation in adult mice ins only marginally affected by fat droplet size

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The production process of infant milk formula (IMF) alters physical properties of fat globules, e.g. a reduced fat droplet size, compared to raw milk (RM). Exposure to a postnatal diet with complex lipid matrix (CLM; contains fat globules with physical properties more closely to RM) prevents excessive diet-induced fat accumulation in adult mice (Oosting et al., 2010). One of the properties of CLM is that it contains larger fat droplets compared to standard produced IMF. Hence, the current study investigates whether dietary fat droplet size by itself affects development of body composition. Postnatally, between 16 and 42 days of age, male C57Bl/6j mice were subjected to a diet containing IMF with a standard fat droplet size (IMF-S; mode 0.5 m) or IMF with large fat droplet size (IMF-L; mode 4.0 m), but no other physical properties of previous mentioned CLM. Subsequently, a moderate Western style diet (WSD, 10 w% fat) was fed until dissection at 98 days of age. Body composition was monitored by dual x-ray absorptiometry at 42, 70 and 98 days of age. Interestingly, although mice on the IMF-L diet showed a lower fat accumulation during adulthood compared to the IMF-S diet, this effect was not significant. Hence, although an increased fat droplet size in the postnatal diet does affect adult body composition, evidently other aspects of the CLM are also responsible for the previously observed prevention of diet-induced fat accumulation during adulthood. Oosting et al., 2010, EARNEST.

III-59  Experimental studies to analyze prenatal programming of obesity later in life by environmental endocrine disruptors

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Endocrine disrupting compounds (EDCs) present in food and drinks are thought to be another factor implicated in the dramatic increase of obesity worldwide. Following the Origins of Health and Disease (DOHaD) principle, exposure to these EDCs during the sensitive perinatal period can program the fetus/neonate towards increased susceptibility to the development of obesity later in life. This altered programming is hypothesized to occur via DNA methylation, an epigenetic mechanism, in target tissues involved in energy homeostasis and appetite regulation, or via altered cell differentiation. In our project, in vivo and in vitro experimental studies are designed to provide observational and mechanistic evidence to support epidemiological associations between exposure to major EDCs in food and development of obesity later in life. In in vivo studies, mice will be exposed to representatives of obesogenic EDCs, starting with bisphenol A (BPA). Dams are exposed via the diet during the premating, mating, gestation and lactation period and offspring are assessed for obesity related parameters. Materials, e.g. DNA from fat tissue, from this and related studies will be examined for epigenetic changes, with method optimization as a first step. In that process, DNA methylation will be measured by CpG island microarray analysis, HPLC and methylation sensitive PCR. Furthermore, in vitro studies, epigenetic and differentiation mechanisms will be studied by differentiating embryonic stem cells into adipocytes and neurons. Preliminary results on the body weight of the offspring exposed to BPA, the differentiation models, and the first results for DNA methylation methods will be presented.

III-60  High protein content of early diet and programming of later adiposity in rats

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Background - Early high protein intake is associated with childhood BMI and weight but its impact on body composition later in life in adult age is not known. Aim - To investigate the long-term consequences of high early protein intake (as carbohydrate or fat exchange) on body composition and glycemia in the rat. Methods - Three groups of male SD rats (n=25) were pair-fed with post-suckling diets varying in protein (casein), fat and carbohydrate as follows: 40, 10 and 50 %E (HP-LF), 20, 10 and 70 %E (AP-LF: carbohydrate exchange), 20, 30 and 50 %E (AP-MF: fat exchange) from age of 2 to 5 weeks. All groups were then fed ad-libitum with a chow diet for 10 weeks, followed by a high fat diet for 31 weeks. Food intake, body weight, body composition and blood variables were measured at different ages. Results - The HP-LF group relative to the other groups with an optimal protein intake (AP-LF and AP-MF) had significantly lower % body fat at age of 5 weeks but developed higher % body fat later at age of 174 days. Furthermore the HP-LF group showed higher plasma IGF-1 relative to both AP-LF and AP-MF groups and higher glycemia relative to the AP-LF group at the end of study: (p<0.05, in all cases). The body weight and energy intakes of all groups were similar. Conclusion - The results provide the first evidence for the programming effect of a high protein intake during the early life and later susceptibility to adiposity and increased glycemia in rodents.

III-61  Roles of thyroid hormones in developing embryos - prenatal exposure to antithyroid drugs and imprinting behaviour in chicks

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Aim: Recent studies in rats have shown that prenatal hypothyroidism due to exposure to antithyroid drugs lead to impaired learning and memory in their offspring. However, there is little understanding of the direct effects of fetal thyroid dysfunction on learning ability without an effect of the mother. In the present study, using a chick embryo as a fetal model, we investigated the effects of
prenatal exposure to antithyroid drugs on imprinting behaviour in hatched chicks. Methods: Twenty mol/egg of methimazole (MMI)
or 5 mol/egg of propylthiouracil (PTU) were administered to eggs on embryonic day 14, while the control was given only a vehicle.
An imprinting test was conducted after the chicks hatched. The day-old chicks were exposed to a rotating training object for 150 min.
The next day, the trained chicks were exposed to the training object and a novel object. The imprinting preference was represented as
a preference score (PS), calculated as the rate of chasing the training object to chasing the training and novel objects. Results: In the
MMI-treated chicks, the PS was 0.68 ± 0.06, ranging from 0.38 to 0.88, which was significantly lower than in the control chicks (0.86
0.04, p < 0.01). In the PTU-treated chicks, the PS was 0.69 ± 0.04, ranging from 0.52 to 0.89, which was also significantly lower than
in the control (0.88 ±0.02, p < 0.001). Conclusion: Our findings suggested that fetal thyroid dysfunction altered brain development,
followed by impaired learning and memory after birth.

III-62 Double insults: Phenotypic consequences of folate depletion during development and high fat intake from weaning.
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The DoHAD hypothesis proposes that nutritional insults in utero result in altered programming of offspring, causing increased
adulthood disease risk. Previously we observed that maternal folate depletion during pregnancy and lactation resulted in adult mice
which were heavier (p=0.016) and had heavier organs (liver, p=0.024; small intestine, p=0.036). We aimed to investigate the hypothesis
that offspring born to folate depleted mothers are more susceptible to increased adiposity, and associated health consequences,
particularly when fed a high fat diet. Female C57BL/J6 mice were assigned randomly to folate-adequate (2mg folic acid/kg) or folate-
deplete (0.4mg folic acid/kg) diets 4 weeks prior to mating. Dams remained on allocated diets during pregnancy and lactation. At
weaning, offspring were randomly allocated to a low (LF; 5%) or high fat (HF; 20%) diet, resulting in 4 treatment groups. Offspring
were weighed weekly and food intake was assessed at 9 weeks of age. Total adiposity and liver fat deposition was assessed by MRI
scanning at 12 weeks of age. HF-fed males, but not females, ate less (p<0.001) than those fed the LF diet. Folate depletion during
pregnancy and lactation did not affect body weight, adiposity or liver fat deposition of offspring. HF-fed females were heavier
(p<0.001) than the LF-fed females, but males body weight was not affected by diet. Total adiposity was increased (p=0.001) in HF-fed
male and female mice and there was a tendency (p>0.05) for liver fat to be higher on the HF diet in both sexes. We thank NuGO and
the BBIRS (BB/G007993/1) for funding.

III-63 Effects of an arachidonic acid - docosahexaenoic acid mixture on the development of obesity and its related disorders
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Arachidonic acid (ARA) and docosahexaenoic acid (DHA) have been proven to support brain development and vision and their dietary
supplementation is therefore considered to be health beneficial, especially during early life stages. This study addresses whether ARA-
DHA supplementation, at relatively low amounts, is effective in reducing the development of obesity and its related disorders. This
was tested in ApoE3L-transgenic mice, a humanized animal model for hyperlipidemia with mild obesity and insulin resistance, which were
fed a high-fat-high-carbohydrate (HFHC) diet. ApoE3L-mice were fed ad libitum with a HFHC-diet (28% fats, 42% carbohydrates) in
the absence or presence of 0.129wt% ARA and 0.088wt% DHA. Food intake, body weight, plasma cholesterol, plasma triglycerides
and fasting glucose and insulin were measured during a 16-weeks feeding period. At the end of the experiment, plasma levels of HDL-
LDL-, VLDL-cholesterol and fat tissue and liver weights were determined. Throughout the feeding period, mice that were fed the
ARA-DHA supplemented HFHC-diet gained less body weight in comparison to the control group with the HFHC-diet only. ARA-DHA
supplementation also lowered plasma cholesterol and fasting glucose levels. At the end of the experiment, ARA-DHA supplemented
mice had a reduced relative liver weight and an increased HDL/LDL-ratio as compared to their controls. No effects of ARA-DHA
supplementation were found on food intake, insulin levels, and fat tissue weights. This study shows that a HFHC-dietary context,
supplementation of ARA and DHA in relatively low amounts has health benefits on body weight, plasma cholesterol, plasma glucose
levels and liver health.

III-64 Changes in rats born at stress periods of different etiology
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Antenatal stress could interfere postnatal life. Earlier we showed that consequences in rat pups development depended on etiology of
antenatal stress. The present investigation is devoted to post-stress changes in pregnant rats. Females on the 9-10th day of pregnancy
were subjected to one of the stressors: acute hypobaric hypoxia (AHH, about 5% O2, rats were divided to low and highly resistant to
hypoxia) or immobilization (IM, for 6 hours). 24 hours after we detected behaviour; parameters of heart rate variability (stress-index
and RMSSD); the level of corticosterone in blood plasma; parameters of GABA-metabolism system (free GABA level, glutamate
hypoxia) or immobilization (IM, for 6 hours). 24 hours after we detected behaviour; parameters of heart rate variability (stress-index
and RMSSD); the level of corticosterone in blood plasma; parameters of GABA-metabolism system (free GABA level, glutamate
decarboxylase and GABA-transaminase activity) in pregnant rats. We found out that only AHH changed behaviour of pregnant rats
in comparison with non-stressed control. Both low and highly resistant females had the increased locomotor and orientative activity
and the decreased anxiety level. Besides low resistant rats showed the increased activity of GABA-transaminase (of 22.2 %) and the
decreased level of plasma corticosterone (of 43.7 %). On the other hand only IM lowered RMSSD (1.7±0.09 after IM compared to
2.06±0.14 in control) indicating the decrease of parasympathetic part in heart regulation.According to data obtained AHH and IM
changed the state of maternal organism in different ways underlying different consequences in rat pups postnatal development.

III-65 Body composition of neonatal piglets during growth
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During studies of neonatal growth it is important to be able to accurately assess changes in body composition. Previous studies have
demonstrated that quantitative magnetic resonance (QMR) provides precise and accurate measurements of total body fat mass, lean mass and total body water in piglets. The purpose of this study was to use EchoMRI for infants instrument to measure changes in the body composition of piglets from birth to about 12 kg. A total of 100 piglets were scanned starting at few days of age and weighting about 2 kg and finally weighting less than 12 kg. The rates of body growth and fat and lean deposition were analyzed by linear regression analysis. The mean (SD) rate of total body growth was 23676 g/d. The rate of fat deposition ranged from 10.6 to 64.9 g/d with a mean of 3213 g/d. The rate of lean deposition ranged from 39.1 to 353.6 g/d with a mean of 18860 g/d. The rates of both fat and lean deposition were highly correlated with total body growth rate respectively. The correlation between the rates of fat and lean deposition was 0.74. The results of this study demonstrate that QMR is a useful method for measuring changes in body composition in piglets. Furthermore, the results indicate that during the period of growth from birth to 12 kg, the rates of both fat and lean deposition are linear and highly correlated with total body growth.

III-66 Altered development and brain of chick embryos by antithyroid drug
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Aim: Deficiency in thyroid hormones during the mammalian fetal development may modify the programming of the differentiation and maturation of tissues, leading to dysfunctions later in life. To evaluate the harmful consequences of hypothyroidism, we produced hypothyroidism in chick embryos by using methimazole (MMI: inhibitor of thyroid hormone biosynthesis), and analyzed their development and biochemical changes. Methods: The fertile hen’s eggs were placed in the incubator at 37.6 ± with 68% humidity (day 0). Typically, chick embryos were treated with MMI (20mol/egg) at day 14, and the growth rate and brain development were subsequently examined on the indicated days before and after hatching. Results: 1) While 94% of control embryos hatched on day 21, 0% and 60% of MMI-treated embryos hatched on days 21 and 24, respectively. 2) MMI retarded the rates of body weight as well as liver and heart, and delayed the hatching. In the day-old chicks, however, the externals and their weights were less noticeable between the untreated and MMI-treated groups. 3) Embryos treated with MMI exhibited increased masses of cerebrum, optic lobe, brain stem and cerebellum at the hatching day. Most notably, the cerebellum resulted in 1.35-fold increase in weight compared to the untreated animals. 4) Acetylcholinesterase activities in the brain parts on the day of hatching were decreased to 0.9-fold of the untreated control. Conclusion: These results suggest that the alterations during the embryonic development by MMI treatment induce the long-term differences in chick behaviour and learning abilities.

III-67 Disruption of ghrelin signaling during early postnatal development has enduring consequences on energy balance regulation in mice.
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Ghrelin is a pleiotropic hormone originally described to promote food intake. Recent data also have indicated that this hormone may be involved in perinatal development. In the present study, we explored the consequences of disrupting ghrelin signaling specifically during early postnatal life on life-long metabolism. The results indicate that anti-ghrelin administration in mice during early postnatal life results in changes in growth as revealed by a significant increase in pre- and post-weaning body weight curves, compared to vehicle-treated animals. These changes in body weight were not associated with changes in length. Nevertheless, animals treated with the anti-ghrelin neonatally had increased adiposity and hyperphagia when they become adults. Together, these data indicate that ghrelin is required for normal perinatal development in mice and that disruption of ghrelin signaling during critical periods of development compromise metabolic regulation. We are currently investigating whether these impaired metabolic regulations are associated with disrupted development of neuroendocrine hypothalamic circuits that control feeding and energy balance.

III-68 The effect of sow back fat and gestation feeding level on serum IGF-I levels of progeny
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Low birth weight and inadequate prenatal nutrition are associated with disease in progeny in later life. The foetuses programmes itself to adapt to poor nutrition in utero. This metabolic programming may involve hyperinsulinaemia, hyperleptinaemia and anomalies in the IG axis. The aim of this study was to determine the influence of (a) back fat levels in gilts and (b) feeding levels during gestation, on serum IGF-I levels in progeny. Gilts with either a low backfat depth (P2 ~11.7 mm) or high backfat depth (fat; P2 ~17.2 mm) were fed a restricted feed level (1.8 kg), normal feed level (2.5 kg) or high feed level (3.5 kg) to day 90 of gestation. All gilts were then fed 2.5 kg to farrowing. Blood samples were collected from light birth weight (<1.2 kg) and heavy birth weight (>1.7 kg) piglets at weaning and at slaughter (~ d 158 of age). IGF-I levels in serum were measured, in triplicate, by ELISA. Data was analysed using the mixed models procedure of SAS with effects of time (weaning or slaughter), birth weight, gestation feeding level and sow back fat. Gilt was included as a random effect. Slaughter weight offspring had higher serum IGF-I levels than offspring at weaning (P<0.001). There was no effect of sow back fat level or gestation feed level on serum IGF-I levels in progeny. High birth weight offspring tended to have higher IGF-I levels than light birth weight pigs (159.89.9 cf. 136.89.2 ng/ml, P=0.09) at both weaning and slaughter.

III-69 Antihyperglycaemic effect of aqueous extract of foeniculum vulgare miller in diabetic mice
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AIMS: Present investigation aims to study the control of blood glucose in alloxan induced diabetic mice METHODS: Method used for extraction was continuous hot percolation method in which Soxhlet apparatus was used.95%ethanol was used as solvent. Male albino mice weighing about 20-25 g obtained from Guru Angad Dev University of Veterinary Science, Ludhiana were used for the study. Diabetes was induced by a single i.p. injection of 125 mg/kg of alloxan monohydrate (S.D Fine - Chem. Ltd., Mumbai, India), in sterile saline (11). After 48 h, animals with serum glucose level above 200 mg/dl (diabetic) were selected for the study. Blood samples
from mice were collected by retro-orbital puncture (ROP) technique. Serum glucose levels were determined by glucose oxidase and peroxidase method using commercially available kit (Medsource ozone Biomedicals Pvt. Ltd., Mumbai). Determination of serum glucose was done at 510 nm on colorimeter. RESULTS: Single administration (single dose) of aqueous extract of fennel (25, 50, and 100 mg/kg, p.o.) in diabetic Swiss albino mice, showed reduction in serum glucose level after 45 min. Maximum reduction in serum glucose level was seen at doses of 100 mg/kg. Aqueous extract of fennel in all doses except 25 mg/kg did not cause any significant decrease in blood glucose. CONCLUSION: It may be said that the aqueous extract of fennel decreased the serum glucose level and improved glucose tolerance owing to the presence of aldehyde moiety. The aqueous extract of fennel has antihyperglycemic activity as it lowers serum glucose level in diabetic mice.

III-70 Metabolic imprinting effect in beef production: Effects of Nutrition manipulation during an early growth stage on the meat quantity in Wagyu (Japanese Black)

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We aim at producing a high-quality safe beef product while maximising the use of domestic grass resources. We would like to apply ‘metabolic imprinting’, which is based on medical research regarding ‘the developmental origins of health and disease (DOHaD)’ to beef production. In this study, we investigate, using molecular biology and histochemistry methods, whether the metabolic imprinting effect of differences in feeding during an early growth influences on the meat quantity of Japanese Black steers or not. The high energy group (HE: n=12) underwent intense nursing (maximum intake of 1.8 kg per day) at 3 months of age and was fed a high-concentrate diet for 3 to 10 months of age. On the contrary, the Roughage group (R: n=11) underwent normal nursing and was fed only roughage ad libitum from 3 to 10 months of age. After 10 months of age, both groups were fed only roughage ad libitum and grazed from 10 to 30 months of age. Samples of tissues from the longissimus muscles in all animals were collected and biopsied at five times (3, 10, 14, 20 and 30 months of age). Gene expression related to muscle development in muscle were measured by real-time PCR. The weight of major muscles and bones, the composition of carcass including major fats, the composition of myofiber type were measured. Finally we also investigated micro array and methylation chip analysis. The statistical analysis of data obtained is in process.

III-71 Hypoglycaemic effect of methanolic extract of Butea Monosperma (Kino) on alloxan induced diabetes

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Diabetes is one of the most chronic diseases in the world affecting nearly 30% population. Experimental animal models in which diabetes was induced by administration of alloxan, streptozotocin, have been used effectively to study etiologies, complications, treatment & prevention of diseases. Synthetic hypoglycemic agents in use can produce serious side effects and they are not suitable for use during pregnancy. Therefore, the search for more antidiabetic of various plants in response to WHO recommendation on diabetes mellitus. METHOD: Butea monosperma(Kino) is to be useful in traditional medicine in the treatment of diabetes in Punjab and Madhya Pradesh. The methanolic extract of B. monosperma was tested for antidiabetic and hypoglycemic activity by GTT (Glucose tolerance test) in normal rats, and alloxan induced diabetic rats. The methanolic extract had shown significant lowering the blood glucose level. There is no effect shown in normal rats with the B.monosperma extract. In alloxan induced (120 mg/kg, body wt.) diabetic rats the maximum reduction in blood glucose levels was observed after 6 hours of oral treatment at a dose of 600mg/kg. The observed activity was compared with standard Glibenclalide (5mg/kg,orally). RESULTS: The percentage decrease of glucose level is observed of methanolic extract with standard glibenclamide were 25% and 40% respectively. CONCLUSIONS: The hypoglycemic effect produced may be due to increased uptake of glucose at tissue level or increase in pancreatic cell function or due to inhibition of intestinal absorption of glucose(due to presence of glycosides/ triterpenoids).

III-72 Evaluation of wound-healing potential of Pterocarpous marsupium heart wood extract in normal and diabetic rats

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Rats treated with 200 mg/kg/day Pterocarpous marsupium heart wood extract had high rate of wound contraction significantly decreased epithelization period, significant increase in dry weight, wet weight and hydroxyproline content of the granulation tissue when compared with the diabetic control and normal control groups. Wound contraction together with increased tensile strength and hydroxyproline content support the use of Pterocarpous marsupium heart wood extract in the management of wound healing in normal and diabetic rats. Keywords: Pterocarpous marsupium; Wound healing; Hydroxyproline

III-73 Moderate maternal nutrient reduction (MNR) disturbs fetal cerebral maturation in baboon

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Long-term moderate caloric reduction ensures health, slows aging and prevents age-associated pathologies (Colman et al., 2009). However, moderate dieting in pregnant women might be crucial for fetal brain development. Aim: To determine effects of chronic 30% global MNR on fetal primate brain neuronal maturation. Methods: Pregnant baboons were either fed ad libitum (controls, n=7) or 70% of weight adjusted ad libitum diet (MNR, n=7) from 0.16 until 0.90 of gestation. After Cesarean section and euthanasia under general anesthesia, fetal brain samples were fixed with 4% paraformaldehyde solution. Tissue sections of the forebrain were stained using the Golgi-technique for estimation of fiber network density, and were immunostained against DCX for migrating immature
neurons, NeuN for mature neurons, synaptophysin for synaptic density and myelin basic protein (MBP) for axon myelination. Specific immunoreactivity (IR) was semi-quantified using an image analysis system. DCX+ and NeuN+ cells were counted. Results: MNR led to an increased number of DCX+ cells and reduced number of NeuN+ cells in the neocortex (p<0.05) in parallel with reduced synaptic density and fiber network density (p<0.01). In association, MNR fetuses showed reduced MBP IR of the superficial white matter (p<0.05). In the striatum, MNR increased DCX IR (p<0.01) in parallel with a loss of NeuN IR (p<0.06) and synaptophysin IR (p<0.01) but enhanced MBP IR compared to controls (p<0.05). Conclusions: The reduced cortical network formation and alterations in brain myelination suggest a delay in fetal cortical development as alterations in cortical connectivity that may potentially impact brain function throughout life.

IV- Consumer attitudes / economic and public health impact studies

IV-1 The effect of diet on children’s mental performance - a qualitative study of perceptions, attitudes and beliefs of parents in four European countries.

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Background: Nutrition is one of the many factors that influence a child’s cognitive development and mental performance. Parents play a key role in the development of children’s food choices and dietary habits. To date, there is little published research on parent’s perceptions of the relationship between diet and mental performance of children. The present study aims to qualitatively examine parents’ perceptions and beliefs about this relationship. Method: The study was conducted in England, Germany, Hungary and Spain. Participants were parents of children aged 4-10 years recruited through state elementary schools. A semi-structured interview schedule was used to conduct interviews with a total of 127 parents. All interviews were thematically analysed using NVIVO8. Results: Four main themes emerged from the interviews with a number of subthemes: ‘physical effects of diet’, ‘mental effects of diet’, ‘healthiness of diet’ and ‘parenting (responsibility, food preferences, dietary habits)’. The mental effects of diet were perceived to be on attention and concentration as well as on children’s mood and behaviour. Negative effects are associated with sugary and fatty foods while positive effects are associated more generally with a healthy balanced diet. Conclusions: In all countries parents perceive attention and concentration to be negatively affected by sugary and fatty foods while a healthy balanced diet is believed to have a positive effect on mental outcomes. A detailed understanding of parents’ perceptions of the relationship between diet and mental performance can provide valuable input for better formulated communication as well as for claims related to specific food products.

IV-2 Consumers’ Intentions Purchasing Organic Foods in terms of Health Concerns, Eating Attitudes and Food Choice Motives

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This study investigated the correlations of five constructs - health concerns, healthy eating practices and attitudes, food choice motives, attitudes toward organic foods - in the formation of behavioural to the purchasing intentions of organic foods. An instrument encompassing health perception, attitudes, habits and personal traits was developed through the comprehensive reviews of the literatures and the assured validity and internal reliability of the contents. The questionnaire was administered to the students of three universities at Daegu,Kyungpook province. A total of 288 questionnaires were collected for a response rate of 96.0%. The correlations of five constructs and purchasing intention were tested simultaneously using structural equation modelling. Healthy eating practices and attitudes toward organic foods were found to be the determinants which directly influence the intention to purchase organic foods. Health concerns didn’t show direct relation to the purchasing intention of organic foods. The hypothesized path from the health concerns to the purchasing intentions was not supported. The results indicated that food choice motives and healthy eating attitudes should be managed to achieve higher behavioural intention to purchase organic foods.

IV-3 Parents’ understanding of mental performance - a qualitative study in three European countries.

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Background: Parents’ belief systems and attitudes are assumed to be cognitive mediators of parents’ interactions with their children which in turn influence a child’s cognitive development. Insight into what parents understand by children’s mental performance (MP) will help to formulate more sensitive communication about the relationship between nutrition and MP. The present work aims to qualitatively examine parents’ understanding of MP. Method: The study was conducted in England (UK), Germany (DE) and Spain.
Parents have direct influence on food choices presented to their children at home. When analysing what parents consider when choosing food for their children it is important to know what factors they perceive to influence a child’s cognitive development and understanding of mental performance (MP). Mental performance was defined in terms of higher cognitive function (e.g. problem solving) whereas this number was lower in the other two countries (19% UK, 10% ES). Conclusions: In summary, the majority of parents express their understanding of MP using general terms. Parents in Germany and England understand MP as being manifested by levels of attention and concentration or a higher order cognitive function. In contrast, parents in Spain think of a child’s intellectual development. Further quantitative research is needed to understand potential differences in parents’ understanding of MP across wider socioeconomic levels.

**IV-4 Mothers’ problems with infant nutrition in Poland**

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New Polish recommendations (2007) on nutritional management of infants raise numerous doubts among mothers, including the time of introducing gluten products and fish to the diet. The aim of the study was to analyse nutritional problems reported by mothers of children in the first year of age. Material and methods: Between 2008 and 2010, a survey was carried out among 125 mothers of children in the first year of age who use nutritional advisory services, by means of a hotline service offered each month. The qualitative analysis of materials from telephone conversations allowed to identify the major nutritional problems encountered by the mothers of infants. Results: From among the surveyed mothers 80% were breast-feeding women. The mothers breast-feeding infants aged 3-6 months (47%) didn’t cope with their own elimination diet and with introduction of complementary feeding for their children. Mothers of children over 6 months old (62%) experienced problems with introducing hypoallergenic diet and principles of nutritional management of children with iron deficiency anaemia. They found specific information, guidelines and instructions very important.

Mothers knew the new recommendations but only 25% of children received food with gluten in the fifth or sixth month of life, and only 3 children received fish when they were 6-12 months old. Conclusions: 1. Mothers’ knowledge of the current infant nutrition principles didn’t have an impact on practical skills concerning the expansion, modification and optimization of their children’s diets. 2. Nutritional advisory services are necessary for mothers to support and strengthen their competence in nutrition.

**IV-5 Parental attitudes to infant feeding and growth: an interview study**

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Background: Systematic reviews have described the consistent association between rapid infant weight gain and subsequent increased obesity risk. Infancy may be a critical period for obesity prevention. In order to develop an intervention to avoid excessive formula milk intake and prevent rapid infancy weight gain, we sought to understand how parents decide on the volumes and frequencies of formula milk feeds, and their attitudes to their baby’s growth. Methods: Thirty-eight UK-based parents (35 mothers) were interviewed using a flexible semi-structured interview schedule and were also asked to complete a questionnaire. Results: Three main themes emerged regarding the volumes and frequencies of formula milk: i) Baby’s appetite (if the baby finished the bottle, more was added to the next feed); ii) Baby’s weight gain (feeds were increased depending on the baby’s weight); iii) Instructions on the formula milk packets. Parents were more concerned about underfeeding and inadequate weight gain than about overfeeding and excess weight gain. The main barriers to reducing formula feeds would be concerns that the baby would cry, be hungry and demand more frequent feeds. Healthcare professionals’ lack of empathy and insistence on following seemingly unreasonable guidelines (e.g. exclusive breastfeeding to age 6 months) resulted in some parents ignoring all received recommendations. Conclusions: Parents’ decision-making processes regarding the quantities of formula milk they offer could over-ride infant satiation cues and result in overfeeding. Interventions to prevent childhood obesity starting in early life should target such behaviours, and should be delivered with empathy, sensitivity and in a non-judgemental manner.

**IV-6 Parents knowledge on what affects children’s mental performance**

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Parents have direct influence on food choices presented to their children at home. When analysing what parents consider when choosing food for their children it is important to know what factors they perceive to influence a child’s cognitive development and understanding of mental performance (MP). The study was conducted in Spain and participants were parents of children aged 4-10 years old recruited in state elementary schools. A card sorting task was developed and used to conduct interviews with a total of 50 parents. Parents were asked about five different groups of influencing factors: Biological, Educational, Social, Environmental and Psychological factors based on evidence from scientific literature. Mental performance was defined in terms of Attention, Learning, Mood and Behaviour. Parents were asked to rate the effect of 18 factors as strong, moderate or no effects on
child’s mental development in relation to each of the chosen aspects of mental performance. Responses were recorded manually, coded and group analysed using Friedman test and Cronbach Alpha test with the SPSS version 15.0. Spanish data reveal that parents perceive the Environmental, Social and Educational group of factors as having most influence on children’s mental performance. **This study is part of the NUTRIMENTHE FP7 EU Project (contract n 212652)

**IV-7 Teacher’s knowledge on what affects children’s mental performance : Spanish model**

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Teachers have an indirect influence on food choices of children at school. They should be aware of the relevance of every type of food to the mental performance of humans in order to know what are the nutrients that help a better neurodevelopment for brain and behavior. The study aimed to examine Spanish teachers’ understanding of the factors influencing children’s mental performance in a qualitative way. This study was conducted in Spain with 17 participant teachers of children aged 4-10 years old recruited in state elementary schools. They were asked, in open interviews, their opinion on what would they consider affecting the mental performance using different questions on the field of Physical, Mental and Social. A total of 12 questions, based on evidences from scientific literature, were asked. Responses were recorded, coded and group analysed using the Nudist-Vivo program version 8.0. A model of research sorted out from the interviews to give a general view about the study. Spanish data reveal that teachers perceive energy’, caffeine and sugar’ and no breakfast’ as short term effects with a negative repercussion on concentration. Also, they explain that sleeping’ have a direct repercussion on energy levels. Otherwise, long term effects came related to mental performance’, mood-behaviour’, physical development’ and well-feeding’. This long term effects seem to have a repercussion in learning and concentration; and in a specific way, it’s a positive effect from well feeding to concentration, mood and behaviour. **This study is part of the NUTRIMENTHE FP7 EU Project (contract n 212652)

**IV-8 Comparison & similarities in 3 European countries : Teacher’s model on the influence of nutrition in children's mental performance**

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To analyse what school teachers consider when teaching about nutrition to their students, it’s important to know what factors they perceive to influence a child’s cognitive development and mental performance. Teachers play a very important role in the development of children’s food education: choices and eating habits for their future-health. The study aimed to examine teachers’ understanding of the factors influencing children’s mental performance in a qualitative way. The study was conducted in Spain, England and Germany and participants were teachers of children aged 4-10 years old recruited in state elementary schools. They were asked, with open interviews, what they thought that could affect the mental performance. A total of 12 questions, based on evidences from scientific literature, were asked. Responses were recorded, coded and group analysed using the Nudist-Vivo 8.0 program. A model of research sorted out from each one of the countries. The comparison of those 3 models extract from the interviews reveals that English teachers talk about Bad feeding practices’ referring to sweet products while the Germans make a clear difference between fats and sugars, pointing out that fats have an influence in energy levels and school performance when, on the other hand, sugars have effects in hyperactivity and concentration. The Spanish teachers seem more focused on sugars and caffeine. The other significant difference comes from the breakfast’s effects: Germans think that it produces short term effects whereas Spanish differ between short-term (concentration) and long term (mental performance) influence. **Study part of the NUTRIMENTHE FP7-EU Project (contract n 212652)

**IV-9 Eating behaviour of preadolescents and adolescents in an urban area in North Western Morocco**

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The aim of this study was to determine the characteristics of the nutritional transition observed in Morocco in a sample of 190 schoolchildren aged 12 to 16 years from 5 schools in Kenitra urban area. Anthropometric measurements and blood pressure were collected. Two groups were distinguished through the use of a test of food quality to studying the impact of environmental factors. Results: Anthropometric information revealed a prevalence of overweight in 9.7% of the sample. This study also revealed that blood pressure increase with body Mass index (r=0.41 for Systolic and r=0.37 for Diastolic blood pressure). Statistical analyse suggested that several environmental factors influenced the quality of adolescents eating behaviour: educational level and father’s working statute, income of households, as well as home spoken language (respectively Odds Ratio = 3.62 , 2.55 , 2.63 , 2.51 ; CI= [1.81-7.19 ] , [1.24-5.24 ] ,[1.39-4.97] ,[1.2-5.28]) . Conclusion: To correct these eating dysfunctions, a nutritional education strategy during this period of growth seems essential. This strategy will stress the spontaneous consumption of green vegetables and fresh fruits; which cannot be carried out without the implication of the family environment.
IV-10  Relation between duration of breast feeding and growth up to 36 months in the Danish SKOT cohort

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Background: Breastfeeding has marked influence on early growth and high growth velocity is associated with increased risk of overweight and life style diseases. Aim: To explore in detail the association between duration of exclusive (EBF) and duration of any breastfeeding (ABF) and growth. Methods: 312 infants were recruited at 9mo. Weight and length were measured at 9, 18 and 36 (ongoing) mo and information on breastfeeding duration was obtained via questionnaires. Height/length-for-Age Z-score (HAZ) and Body-Mass-Index-for-Age Z-score (BAZ) were calculated (WHO standards). Results: Median duration of EBF was 4.2mo (25 and 75percentile: 3.0 and 4.9mo) and ABF 8.4mo (5.4 and 11.0mo). At age 9mo 55% were still breastfed (BF=9mo). Mean HAZ at age 9, 18, 36mo were approximately 0.3 z-score lower (all p<0.05) among children BF=9mo compared to children BF<9mo. This also applied to mean BAZ at age 9 &18 mo (both -0.3 z-scores and p<0.01), but not 36mo. Duration of EBF was negatively associated with BMI at 18mo (p<0.01, adjusted for birth weight), while this was not the case for duration of ABF. Conclusion: Length/height of infants BF=9mo was close to WHO standards and significantly lower also at 36mo than of those BF<9mo. Those BF=9mo were also thinner at 18mo, but not at 36mo. Interestingly, the effect of duration of EBF had a stronger effect on early increase in BMI than duration of ABF, which could suggest a role of introduction of complementary feeding. These effects of breastfeeding are likely to be important for later obesity.

IV-11  Screening the pregnant mother for hypothyroidism

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Introduction: Deficiency of iodine results in impairment of neuronal development. Vulnerable group are the pregnant women, who live in endemic areas, as their demand for iodine increases (300-350 mcg of iodine /day). In pregnancy, the deficiency remains undetected due to sub clinical hypothyroidism. Objective: To assess the need for screening the pregnant mother for hypothyroidism. Methods: The present study has been focused on screening of pregnant women (185) for hypothyroidism in urban (68) and rural(117) Vadodara. Urine and blood samples of all these subjects were subjected for biochemical analysis. Results and Discussion: Urinary iodine excretion revealed, out of 185 subjects 115 were Iodine deficient. Trimester wise assessment revealed 62.5% were deficient in 1st, 54% in the second and 68.6% in the 3rd trimester. 7% of the subjects were found anaemic. TSH,TT4,FT4,Tg, TPO-Ab analyzed revealed mild increase in TSH and TT4 levels, suggesting subclinical hypothyroidism; FT4,Tg, TPO -Ab showed the results in normal range, suggestive that, the unbound thyroxin circulating in the body was contributive for growth and development of the fetus. Thus the study justifies the need to screen pregnant women for their thyroid hormones as they predict fetal growth and development indirectly. Initiating the thyroid screening programme would be beneficial for the women of reproductive age group.

IV-12  The optimisation of L.casei to laboratory conditions for folate analysis

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RATIONALE AND OBJECTIVE: In the present folic acid deficiency is progressing at an alarming rate and is implicated in a wide variety of disorders from Alzheimer’s to coronary heart diseases, osteoporosis, increased risk of breast and colorectal cancer, poor cognitive performance, hearing loss and the most prevalent Neural Tube Defects. The existing data are based on assay procedures which are known to underestimate folate. Hence the present study was carried with updated trienzyme extraction involving microbiological assay. L.casei (ATCC 7469) is used as the assay organism. The nature of food chosen for analysis, type, state, origin of foods differs for various sources. Therefore, optimization is essential before actual analysis of food sources is carried out. MATERIALS AND METHODS: L.casei (ATCC 7469) was procured from Department of Microbiology, University of New South Wales, Sydney, Australia. To get the desired growth of the organism trials with variations in culture volume (0.1-2 ml), inoculum load (50-1000), alterations in Incubation time (16-22 hrs) and pH (6.1 and 6.8) were carried out. RESULTS AND FINDINGS: The required R-square values=0.99 was obtained. After optimization, the most commonly consumed fruits in Coimbatore, South India were analysed. CONCLUSION: There is much limited data on folate content of foods in India. Hence optimization helped us to analyse the folate content. Key words: Folate, L.casei, Optimization, Microbiological assay, Fruits

IV-13  Seasonality and the maternal factors influencing birth weight – a study in urban slums of Delhi

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Secondary data were gathered from a Government Hospital in Delhi for the years 1989,1998 and 1999 (n = 33,786) and a Government Maternity Center for five consecutive years (1997-2001;n = 2769), wherein all available data relating to various parameters including birth weight were gathered. In addition, longitudinal data (primary) were obtained from 201 pregnant women from urban slums enrolled at 18±2 weeks of gestation and followed at 24+2, 30+2 and 36+ weeks of gestation. To assess seasonal variations in dietary intake of women from LSES, dietary data were gathered from 50 NPNL women round the year. Secondary data indicate that the babies born in February - March had the highest while those born in August had the lowest mean birth weight, while the incidence of LBW deliveries was the minimum during March and the highest in August (p< 0.05). Data further indicate that the birth weight was significantly affected by the maternal age, pre-delivery body weight, haemoglobin status, parity, period of gestation and PIH (p<0.05). These findings were corroborated by the primary data, which conclusively show that maternal nutritional status is a key factor in the outcome of pregnancy. Further, seasonal availability / accessibility of fresh vegetables (including GLV’s) and fruits at affordable prices
IV-14 The first integrated software for approaching a nutritional, clinical and blood profiles
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Background: Data from intake survey is usually managed independently in stages (annotate/record/analysis). Likewise, a clinical and lab data approach is separated. It entails a great deal of time-consuming and failure risk. The aim was to develop an all in one’ computing program to solve these problems together. Methods: A web format application computer has been developed, based on a 3 module configuration. MODULE 1: data intake registration, which enables patients to fill it in. The collection and saving data are simultaneous. MODULE 2: data processing, which transforms food into nutrients, using food-composition standardised tables. MODULE 3: nutritional data integration with clinical and blood profile (lab data) imported from any LIS (Laboratory Information System, connected to auto analyzers). Results and conclusions: This program (called EURISCAPIQ) optimizes resources: less time consuming and better data quality control (traceability process, fewer steps and fewer pitfalls), so it improves cost-effectiveness in nutritional studies. To unite database annotation and integrative data analyses made to consider artificial intelligence modes as expert rules or even genetic algorithms. For example: EURISCAPIQ has an early warning system when intake limit is exceeded (nutrients/calories) and linking with serum concentrations (cholesterol, triglyceride, etc.). It may be based on different diseases. Web format allows it to be used from anywhere without software installation. This characteristic is not considered by other authors’ programs so it is an innovation (Bermejo Viedo, 2005) (Paschidi, 2006) (Yu-jin, 2007) (Gutierrez Bedmar, 2008) (Buisson, 2008). Integrative data management software to study nutrition and blood profile relationships was unpublished too.

IV-15 Nutrition as an osteoporotic factor among females in Alexandria, Egypt
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Osteoporosis is an escalating disease and is considered, a major health concern around the world. This study was done in Alexandria city among 80 females comprising 40 women and 40 girls, chosen accidentally from one of the sports club in Alexandria. Their dietary intake, nutrition knowledge, and their bone health were investigated to find out any possible relation between their bone health and their nutritional status, and nutrition awareness, and some personal characteristics, as well as their life style, and their smoking habits. The required data were collected using a personal interview questionnaire, including socioeconomic and biological characteristics, dietary history, frequency of eating food groups, as well as 24 hour dietary recall method. Anthropometric measurements were determined and BMI was evaluated. Dietary food groups and intake frequency were evaluated using a proposed scoring system. Some biological data were collected including menstruation status, number of pregnancies, lactation practices, menopause age, health history and medical therapy, smoking status, and physical activity. Details of bone pain, history of past fractures and it’s risks, medical treatment, use of hormones, use of vitamins and calcium supplements were also collected. The results indicated that there was low awareness of nutrition as related to osteoporosis incidence. Significant relations existed between bone status and some personal factors like age, menopause and physical activity while differences were highly significant for nutrients intakes especially calcium and vitamin D. Around 85%, 10%, and 5% of the girls and 17%, 30%, and 53% had normal, osteopenic, and osteoporotic bones respectively.

IV-16 Ethnomedicinal Survey of the Santal Tribe Residing In Thakurgaon District, Bangladesh
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The Santals are one of the largest tribes of Bangladesh residing in the northern districts of Thakurgaon, Dinaipur, Panchagarh and Rajshahi. Since very little is known of the traditional medicinal practices of the Santal traditional healers, the objective of this study was to conduct an ethnomedicinal survey of Santal traditional healers among the Santals of Thakurgaon district, Bangladesh. Interviews of the healers were conducted in the local language following obtaining informed consent from the healers. The healers pointed out plants and described their uses. Plant samples were collected and identified at the Bangladesh National Herbarium. The various plant species used by the healers (with ailments treated given in parenthesis) included Cissus quadrangularis (fractures), Clerodendrum viscosum (helminthiasis), Cannabis sativa (bloating), Hibiscus rosa-sinensis (premature ejaculation), Syzygium cumini (diabetes), Heliotropium indicum (cataaract), Scoparia dulcis (diabetes), Anthoncephalus chinensis (swelling), Dolichos lablab (tollittis), Citrus grandis (head deformities in children), Streblus asper (elephantiasis), Oxalis lobata (presence of white mucus in stools), Jatropha gossypifolia (dysentery), Datura stramonium (swelling of finger), Azadirachta indica (large abscess), Momordica charantia (coughs, mucus, body ache), Mikania cordata (dengue fever), Solanum indicum (dehylity), Glycosmis pentaphylla (pain during urination in children), Urena lobata (pain in scrotum), Abutilon indicum (rheumatism), Coccinia cordifolia (mental depression, blood dysentery), Emblica officinalis (appetite stimulant), Cyperus rotundus (any type of gastrointestinal disorders), Euphorbia tirucalli (rheumatic pain), Cinnamomum tamala (biliary disorders), Nyctanthes arbor-tristis (constipation in children), and Cinnamomum verum (low sperm count). It is expected that scientific studies conducted with the plants can lead to discovery of novel drugs.
**IV-17  Pediatrics health administration in care of children with development problems**

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**BACKGROUND:** The healthcare organizations need individuals with vision and judgment to face various economic, ethical, and social issues as well as the financial demands of the complex field in delayed development of children. Multidisciplinary in nature, academic programs in healthcare management are found in a variety of settings, including schools of business, public health, allied health, public administration, medicine, nursing, and health professions.

**METHODS:** Throughout this study, we have had acquire tools and techniques that will increase ours effectiveness and expand your opportunities within our current paediatrics position in outhospital care children with development problems. Children with the most intense needs and their families often cross several public systems, and may enter services and supports that reflect system of care values through any one of them.

**RESULTS:** The impact of these increased resources on health outcomes has been mixed. This public health approach helps to build more stable communities and redirects scarce resources to interventions that are less costly than those needed for youth who already have developed serious physical and emotional disturbances. The risk factors identified in our study should prove useful for designing preventive strategies, thereby improving the quality of care.

**CONCLUSION:** Paediatricians and primary care providers in managed care settings assume an even greater responsibility to identify manage and refer children with all kind of disorders.

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**IV-18  Compritive knowledge of breast self examination in midwifery and nursing student**

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Introduction: breast cancer is the most common type of cancer among women world wide ranking second in mortality from cancer. Bse is a screening method that should be taught at an early age so as to educate women about the importance of early detection of breast cancer. Aim: the aim of this study was to evaluate the level of knowledge of midwifery and nursing student regarding breast self-examination. Materials and methods: this study is descriptive on 23 midwifery and 69 nursing student, data collection tool was a questionnaire the included6 questions about demographic characteristics, and 14 question about knowledge breast self-examination. Data analyzed by descriptive statistics. Result: our results show that the average age being (21-35),majority of them are single (%67/4)and (%29/3) twin. Our result showed no significant differences in midwifery and nursing knowledge.(p>5%). Our result showed the students of midwifery and nursing have mild knowledge. Conclusion: it seems that despite of the importance of the bse in early diagnosis of breast cancer the majority of women have poor knowledge and practice about BSE. Based on the positive attitude of most women about BSE ,it is that increasing the knowledge of women by education ways of breast cancer ,especially BSE ,this will be available by more attention of public health centers, TV and newspaper for increasing women awareness. Key word: breast,student,cancer,self examination
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Hotel Reservation
EUROKONGRESS has reserved room allotments for the conference in different hotels. Please contact the conference office onsite for any questions regarding hotel reservation.

Liability
The organiser cannot be held responsible for any personal injury, accident, damage to private property or additional expenses incurred as a result of changes of dates, venue, programme or else.

Media Center / Oral Presentations
The media center is located in the registration area at the main entrance of the auditorium section.

Opening Hours
Thursday, 6th May 08:30 - 18:00h
Friday, 7th May 07:30 - 18:00h
Saturday, 8th May 08:00 - 13:00h

Important Information
- Oral presentations must be held by the first author of the submitted abstract
- Slide projection will not be available
- No own laptops will be accepted as it may not be compatible with the equipment onsite
- Presentations should be created in PowerPoint 2003 or PowerPoint 2007 (XP) using the ‘Pack and Go’ feature of PowerPoint
- We kindly ask you to save your presentation on a USB stick or CD-ROM and to hand it over to the Media Center staff at your earliest convenience (two hours prior to your scheduled presentation at the latest)
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- Please ensure to be at the lecture hall at least 15 minutes before your session starts

New Investigators’ Award
The New Investigators’ ceremony will be held on Friday, 7th May during the Conference Dinner at the Augustiner Keller. The winners have been informed separately.

EACCME / CME Accreditation
This conference is accredited with 15 European CME credits (ECMEC) by the European Accreditation Council for Continuing Medical Education. Please contact the Registration Desk onsite for certificates of attendance and further information. The ‘Early Nutrition Academy, project Earnest and DOHaD society’ is accredited by the European Accreditation Council for Continuing Medical Education (EACCME) to provide the following CME activity for medical specialist. The EACCME is an institution of the European Union of Medical Specialists (UEMS), www.uems.net. The ‘Power of Programming - Developmental Origins of Health and Disease’ is designated for up to 15 hours of European external CME credits. Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity. EACCME
credits are recognised by the American Medical Association towards the Physician’s Recognition Award (PRA). To convert EACCME credit to AMA PRA category 1 credit, contact the AMA.

Poster Exhibition
The poster areas are located on the 1st and on the 2nd floor of the auditorium section (please see floorplan):
I  Clinical Studies
II  Epidemiology
III  Animal, cell and molecular studies
IV  Consumer attitudes / Economic and public health impact studies
Posters have to be mounted on Thursday, 6th May by 14:00h. Each poster board will be numbered with the personal poster number. Presentation is requested during the whole conference as the poster viewing is scheduled accompanying the entire programme. Posters must be removed on Saturday, 8th May by 15:00h at the latest. Posters which have not been removed by this deadline will be subject to disposal - neither the organiser nor the Klinikum Grosshadern is responsible for removing and handing back posters.

Poster Desk
All necessary materials needed to fix the posters will be provided at the Poster Desk located on the 1st floor. The poster desk is open on Thursday, 6th May from 8:30h – 14:00h.

Guided Poster Tour
The posters of distinction will be introduced by the first authors during the Guided Poster Tour on Friday, 7th May from 13:25h to 14:25h. After a short introduction by the Chair each poster will be presented in a 5 minutes' talk. The authors are requested to be in the poster area at least 15 minutes before the guided tour starts.

Public Transportation to the Conference Venue
From the central station: please take the subway line U1 (direction “Mangfallplatz”) or U2 (direction “Messestadt Ost”) to Sendlinger Tor (one stop from the Hauptbahnhof / central station) and change to the subway line U6, terminus “Klinikum Grosshadern”.
From downtown (Marienplatz): subway line U6 to terminus “Klinikum Grosshadern”.
It is possible to purchase public transport tickets at a reduced price at the registration desk.

Registration Fees

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<thead>
<tr>
<th>Standard Registration Fee</th>
<th>280 EUR</th>
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<tr>
<td>EARNEST/co-sponsoring societies*</td>
<td>260 EUR</td>
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<td>(only for EARNEST Partners and members of DOHaD, DGE, EANS, ESPGHAN, ISSFAL)</td>
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<tr>
<td>Students*</td>
<td>170 EUR</td>
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*A proof has to be provided.

The conference fees include the participation in the scientific sessions, coffee and lunch breaks, the Welcome Reception on Thursday evening as well as the Conference Dinner on Friday evening.

Onsite payment can either be made in cash or by credit card.

Session Halls
All session halls are located on the 1st floor.

Travel by Car
Since 1st October 2008 Munich has a low emission zone. High-emission vehicles are no longer allowed to drive in the city center. A sticker will be required to prove that your vehicle fulfills the EU exhaust standards. The new regulation covers all automobiles, buses, motor homes and trucks.

Wardrobe
The wardrobe can be found in the registration area of the conference venue. Please note that the organisers cannot provide security staff or other means to attend property left at the wardrobe and cannot be held responsible for damage or loss of property left at the wardrobe.

Social Programme

Welcome Reception
On the first conference evening all participants are warmly invited to the Welcome Reception in the city center.

Location: Ludwig-Maximilians-University
Main Building
Geschwister-Scholl-Platz 1, 80539 Munich
(subway station „Universität“, subway line U3 or U6)

Date/Time: Thursday, 6th May 2010 at 19:00h

Price per person: included in the registration fee
separate registration necessary
(subject to availability)

Dress Code: Business attire

Conference Dinner/Bavarian Evening
On Friday night we will celebrate a Bavarian Evening with traditional food and entertainment in a relaxed atmosphere.

Location: Augustiner Keller München
Arnulfstr. 52, 80335 Munich
(fast train / S-Bahn station „Hackerbrücke“, tram 16 or 17)

Date/Time: Friday, 7th May 2010 at 19:30h

Price per person: Participants: included in the registration fee (dinner and 2 drinks)
separate registration necessary
(subject to availability)
Accompanying persons: 50 EUR incl. 2 drinks
(subject to availability)

Dress Code: Casual or Traditional Costumes
If you feel comfortable, then we have done our job well

You hold your meeting – we organize it

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