EARLYNUTRITION
Long-term effects of early nutrition on later health

EARLY NUTRITION ACADEMY

THE POWER OF PROGRAMMING 2014

International Conference on Developmental Origins of Adiposity and Long-Term Health

March 13 - 15, 2014 Munich, Germany

PROGRAMME AND ABSTRACTS

In collaboration with

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THE POWER OF PROGRAMMING

International Conference on Developmental Origins of Adiposity and Long-term Health

Campus of the University Hospital, Munich-Großhadern
http://munich2014.project-earlynutrition.eu/

Munich, Germany
13th - 15th March, 2014

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Welcome to Munich and to "The Power of Programming 2014 - Developmental Origins of Health and Disease"

On behalf of the Early Nutrition Project Consortium, the Scientific Committee and the Local Organizing Committee, I am delighted to welcome you to this international conference. Strong evidence has accumulated to show that environmental cues, including nutrition before and during pregnancy and in early childhood, have important long-term effects on development, performance and other health outcomes including obesity and associated disorders. Epidemiological observations are increasingly supported by experimental studies exploring biological mechanisms, as well as by prospective intervention trials providing indisputable 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. 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. In a multidisciplinary approach, outstanding leaders in the fields of developmental origins, biological and clinical sciences, nutrition, epidemiology, epigenomics, metabolomics and more present the latest knowledge in their fields. Abstract presentations provide most recent findings. Further exciting features of the programme are a "Meet the Professors – Career Building session" and a dedicated "New Investigators Forum" to foster skills and the personal development of emerging researchers of excellence. We trust there will be unique opportunities for trans-disciplinary and global research interactions and the development of further, refined study approaches, and for preparing steps towards translational application into policy and practice. Thereby, we hope that this meeting will contribute to achieving better health outcomes for future generations.

We are most grateful indeed that this meeting was made possible with financial support by the General Directorate Research of the European Commission as part of the European EarlyNutrition Research Project (www.project-earlynutrition.eu), and by the German Research Council (Deutsche Forschungsgemeinschaft) as well as further sponsors and the help of the Ludwig Maximilians University of Munich. 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 the improvement of early nutrition.

We hope you enjoy the Conference and benefit from it, and we wish you a very pleasant stay in Munich!

Berthold Koletzko

EarlyNutrition Coordinator and ENA Managing Director

Brigitte Brands

Scientific Director and Scientific Project Manager EarlyNutrition

Simone Cramer

Conference Secretary and Administrative Manager EarlyNutrition

Welcome from Dr. Isabelle de Froidmont-Görtz,

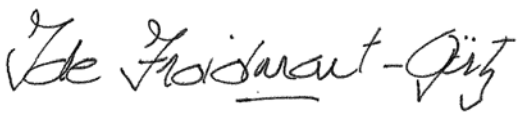
Unit Agri-Food Chain, DG Research and Innovation, European Commission

Europe 2020, with its triple objectives of smart, sustainable and inclusive growth, is the Union's strategy for successfully exiting the financial and economic crisis and re-taking the path towards sustainable growth. In this respect, fiscal consolidation and structural reform measures are needed for short term stabilisation of the economy, but they are not sufficient to ensure long-term growth. This requires strong investment in research and innovation, which is also needed to address pressing societal challenges such as climate change, ageing population, or the move towards a resource efficient society. Such investment offers direct stimulus to the economy, as well as being vital to securing an excellent knowledge base and a competitive industry. It is the only way for Europe to remain competitive in a globalised world, drive economic growth, create jobs and sustain high standards of wellbeing.

Horizon 2020 which is the biggest EU Research and Innovation programme ever with nearly €80 billion of funding available over 7 years (2014 to 2020) promises more breakthroughs, discoveries and world-firsts by taking great ideas from the lab to the market. Horizon 2020 is the financial instrument to implement the innovation Union, one of policy priorities of the Europe 2020. By coupling research and innovation, Horizon 2020 will put emphasis on excellent science, industrial leadership and societal challenges. The goal is to ensure Europe produces world-class science, removes barriers to innovation and makes it easier for the public and private sectors to work together in delivering innovation.

In the Seventh Framework Programme for Research and Technological Development (2007-2013), the Commission funded several research projects to better understand the relationship between diet, lifestyle and health across the lifespan. Through societal challenges 'Health, demographic change and well-being' and 'Food security, sustainable agriculture and forestry, marine, maritime research and inland water research and the bioeconomy', Horizon 2020 will continue to explore food and diet as the main factors for promoting and sustaining health and well-being and for reducing the risk of diseases development.

This conference on the power of programming will present the latest results of the successful EU project EARLY NUTRITION (Long term effects of early nutrition on later health) aiming at exploring key hypotheses on likely causes and pathways to prevention of early life origins of obesity and associated disorders. This pioneering conference on developmental origins of adiposity and long term health will provide the ideal platform for a critical review of current knowledge in the field. It will also give the opportunity to identify future research needs addressing global challenges such as guaranteeing food security while adapting to a changing climate, reducing the environmental impact of agriculture and industry, and maintaining an affordable, safe, healthy and nutritious food supply. I wish to all of you a fruitful and successful conference.



Dr. Isabelle de Froidmont-Görtz

Unit Agri-Food Chain
Directorate General for Research & Innovation
European Commission

Welcome from Melanie Huml

Bavarian State Minister of Public Health and Care Services

Ladies and Gentlemen,

Overweight and obesity cause more deaths worldwide than malnutrition and undernourishment. They have doubled in frequency over the last 30 years, and more than half of all adults in Germany are now affected. Childhood and adolescent weight problems are becoming increasingly widespread, along with all their consequences for physical and mental health. Overweight significantly increases the likelihood of cardiovascular diseases, diabetes, and cancer – the greatest causes of sickness in our society. This trend is alarming, and that is why effective prevention is one of the core elements of Bavaria's health policy.

We have long known that we can reduce our individual risk of overweight and obesity through proper diet and regular physical activity. This is why it is a matter of conviction for the Bavarian State Ministry of Public Health and Care Services to support numerous projects that motivate people in Bavaria to lead healthy lifestyles. These efforts focus particularly on proper nutrition during pregnancy and early childhood. With good reason, the importance of this issue for later health development is drawing ever more public attention. It is to the credit of scientists at the Ludwig-Maximilians-Universität of Munich that significant contributions to research on this topic have come from Bavaria.

This work can be continued with The Power of Programming 2014 component of the EarlyNutrition international research programme. I am also very much looking forward to the conference as it is more than an essential contribution to effective obesity prevention in the future. It is truly a part of our future inasmuch as it champions the health of our young people. With this in mind, I wish all of the conference participants much joy, new ideas, and every success as they continue their work.

Yours sincerely

Melanie Huml

Melanie Huml

Bavarian State Minister of Public Health and Care Services

Welcome from Prof. Bernd Huber

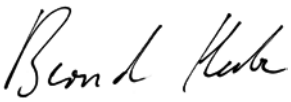
President of Ludwig-Maximilians-Universität Munich

It is a great pleasure for me to welcome you at Ludwig-Maximilians-Universität München for the international conference on "Developmental Origins of Adiposity and Long-Term Health". As one of the leading research intensive universities in Europe with a more than 500-year-long tradition, it is LMU's mission to combine excellent research with outstanding teaching, to conduct basic research and tackle the grand societal challenges of our time. Therefore research of LMU's medical faculty has one of its main focuses on the treatment and prevention of common diseases.

As one of the big third-party funded projects coordinated by the LMU, "EarlyNutrition" addresses such a serious health concern: the increase of overweight children worldwide. After the great success of the preliminary Early Nutrition Programming Project (EARNEST), in 2012 Prof. Berthold Koletzko and his colleagues again applied successfully for EU funding.

During this conference over ninety renowned speakers will present their most recent research results and discuss manifold aspects of this topic. Personal contacts which result from participating at this conference are very important for mutually beneficial exchanges on questions of scientific and clinical relevance, and the conference program offers many opportunities to deepen discussions in a stimulating environment.

LMU is pleased to host this international conference again, four years after the great success of the first meeting which was joined by nearly 600 participants. I wish all participants a successful conference with a fruitful exchange of ideas and many occasions for networking with your colleagues. Enjoy your stay in Munich.



Prof. Dr. Bernd Huber

President of LMU München

Meeting Organiser

Project EarlyNutrition and the Early Nutrition Academy (ENA)

in collaboration with the:
Developmental Origins of Health and Disease Society
European Society for Paediatric Gastroenterology, Hepatology and Nutrition
German Society of Nutrition
International Society for the Study of Fatty Acids and Lipids
Internation Union of Nutritional Sciences
World Association of Perinatal Medicine

Meeting President

Berthold Koletzko

Professor of Pediatrics
EarlyNutrition coordinator and ENA Chairman
Ludwig-Maximilians-University of Munich, Germany

Scientific Committee

Prof. Berthold Koletzko, Conference Chair (EarlyNutrition)
Ludwig-Maximilians-University of Munich Medical Center, Germany

Dr. Brigitte Brands, Scientific Director (EarlyNutrition)
Ludwig-Maximilians-University of Munich Medical Center, Germany

Prof. Patrick M. Catalano (EarlyNutrition)
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Ludwig-Maximilians-University of Munich Medical Center, Germany

Prof. Gernot Desoye (EarlyNutrition)
Medical University Graz, Austria

Prof. Jodie Dodd (EarlyNutrition)
University of Adelaide, Australia

Prof. Ibrahim Elmadfa (IUNS)
University of Vienna, Austria

Prof. Sonja Entringer (EarlyNutrition)
University of California, USA

Prof. Matthew Gillman (EarlyNutrition)
Harvard Pilgrim Health Center, USA

Prof. Keith Godfrey (EarlyNutrition)
University of Southampton, UK

Prof. Hans van Goudoever (ESPGHAN / EarlyNutrition)
VU University Medical Center Amsterdam,The Netherlands

Prof. Ute Nöthlings (DGE)
Christian-Albrechts-Universität zu Kiel, Germany

Prof. Wendy Oddy (EarlyNutrition)
Telethon Institute for Child Health Research,
University of Western Australia, Australia

Prof. Lucilla Poston (EarlyNutrition)
King's College London, UK

Dr. Richard Saffery (EarlyNutrition)
Murdoch Children's Research C

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Medical University of Warsaw, Poland

Scientific Information

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Friday, March 14, 12.30 – 13.30
Nestlé Nutrition Institute Lunch Satellite Symposium:
"Protein – Growth – Special needs"
Lecture Hall II

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Saturday, March 15, 14.30 – 18.00
DSM Satellite Symposium:
"Meeting Nutrition Needs in the first 1,000 Days of Life"
Lecture Hall IV

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iFamily
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The Power of Programming – Developmental Origins of Adiposity and Long-Term Health

Scientific Programme

Thursday, 13th March 2014

10.00 – 10.45 Lecture Hall III + IV	**Opening Session: Welcome Notes and Introduction** **Isabelle de Froidmont-Goertz** (Unit for Agri-Food Chain, DG Research and Innovation, European Commission) **Melanie Huml** (Bavarian State Minister of Public Health and Care Services) **Berthold Koletzko** (EarlyNutrition coordinator, Ludwig-Maximillians-University of Munich)		
10.45 – 11.30 Lecture Hall III + IV	**Plenary session I:** *Chair: Lucilla Poston* **The LIMIT Randomized Trial** – Jodie Dodd (Adelaide, Australia)		
11.30 – 11.50	***Coffee and Tea Break***		
11.50 – 13.25 **A.1:** Lecture Hall III **B.1:** Lecture Hall II **C.1:** Lecture Hall IV	**A.1 Parallel Session** **Glycaemic Load in Pregnancy – Opportunities for Prevention?** *Hosts/Chairs: Cristina Campoy, Christina Sherry* • The UPBEAT study: a lifestyle intervention study in obese pregnant women – *Lucilla Poston (London, UK)* • *A pilot study to evaluate the effects of a dietary supplement with slow digesting-low GI carbohydrates in obese pregnant women using continuous glucose monitoring – Nashita Patel (London, UK)* • Dietary and physical activity interventions for women who are overweight or obese during pregnancy – The findings of the LIMIT randomized trial *– Jodie Dodd (Adelaide, Australia)* • *Maternal and fetal predictors for the therapy-management by gestational diabetes – Tanja Groten (Jena, Germany)* • Maternal nutrition and fetal health *– Fionnuala McAuliffe (Dublin, UK)*	**B.1 Parallel session** **Metabolic Predictors of Maternal and Childhood Obesity** *Hosts/Chairs: Louise Kenny, Christian Hellmuth* • Fatty acid composition in blood and obesity in childhood – *Marie Standl (Munich, Germany)* • *Metabolomic profiles of childhood obesity – Wei Perng (Boston, USA)* • Influence of early nutrition on metabolic processes – investigated by targeted LC/MS based metabolomics *– Christian Hellmuth (Munich, Germany)* • *Evaluation of ursodeoxycholic acid (UDCA) to ameliorate maternal cholestasis-induced metabolic abnormalities in the fetus and offspring – Georgia Papacleovoulou (London, UK)* • Metabolic pathways to diabetes and obesity *– Matej Oresic (Finland)*	**C.1 Parallel session** **Does the Placental Function Contribute to Fetal and Childhood Adiposity?** *Hosts/Chairs: Sylvie Hauguel-de Mouzon, Christian Wadsack* • Lipid-immune crosstalks at the maternal-fetal interface: impact of obesity *– Sylvie Hauguel-de Mouzon (Cleveland, USA)* • *A periconceptional maternal hyperglycemia disrupts the feto-placental membrane fatty acid profiles in a rabbit model – Delphine Rousseau-Ralliard (Jouy en Josas, France)* • Placental fatty acid transfer - a key factor of fetal growth – *Elvira Larque (Murcia, Spain)* • *Exercise before and during an obese mouse pregnancy restores some placental gene expression and transport function – Geraldine Gascoin (Cambridge, UK)* • Placental transport and metabolism of amino acids *– Rohan Lewis (Southampton, UK)*

Thursday, 13th March 2014 (continued)

13.25 – 15.00	**Lunch Buffet + Poster Viewing**	**14.00 – 14.50** **"Meet the Professors"** **1. Intervention studies in pregnancy** – *Lucilla Poston, Jodie Dodd, Fionnuala McAuliffe* **2. Intervention studies in infancy** – *Hans van Goudoever, Piotr Socha* **3. Epidemiology** – *Vincent Jaddoe* **4. Mechanistic studies in animals** – *Susan Ozanne, Julie Owens, Mike Symonds* **5. Epigenetics** – *Richard Saffery, Keith Godfrey* **6. Career Opportunities in Industry** – *Eline van der Beek, Ricardo Rueda* - ZEUS Study Centre -	
15.00 – 15.45 Lecture Hall III + IV	**Plenary Session II:** *Chair: Gernot Desoye* **Epigenetics as the Major Mediator of Fetal Programming: Are we There Yet?** – Richard Saffery (Melbourne, Australia)		
15.45 – 16.15	***Coffee and Tea Break***		
16.15 – 17.50 **A.2:** Lecture Hall III **B.2:** Lecture Hall II **C.2:** Lecture Hall IV	**A.2 Parallel session** **The Influence of Stress and Stress-Nutrition Interactions during Pregnancy on Offspring Adiposity** *Hosts/Chairs: Sonja Entringer, Nick Harvey* • Influence of diet and lifestyle during pregnancy on offspring bone mass and body composition – *Nick Harvey (Southampton, UK)* • *The maternal ingestion of sugar, fat and sodium during pregnancy is associated with the adiposity of children up to 18 months – Liliana Ladino (Granada, Spain)* • Fetal glucocorticoid over-exposure: The key to developmental programming? – *Jonathan Seckl (Edinburgh, UK)* • *Do even psychological pathways exist between certain perinatal factors and childhood obesity? – Eva Kovacs (Pecs, Hungary)* • Interactive effects of stress and lifestyle during pregnancy on offspring body composition, metabolic function – *Pathik Wadhwa (California, USA)*	**B.2 Parallel Session** **The Role of Paternal Factors in Determining Offspring Outcome** *Hosts/Chairs: Susan Ozanne, Hazel Inskip* • Parental body mass index and childhood cardiovascular risk factors – *Romy Gaillard (Rotterdam, Netherlands)* • *Transmission by paternal line inheritance of metabolic and cardio-renal dysfunction to F2 offspring born to a growth restricted father – Mary Wlodek (Melbourne, Australia)* • Genetic determinants of infancy and early childhood growth – *Ken Ong (Cambridge, UK)* • *Paternal consumption of a selenium-deficient diet programs the susceptibility of female offspring to mammary carcinogenesis – Luiza Guido (São Paulo, Brazil)* • Paternal obesity, interventions and mechanistic pathways to impaired metabolic health of offspring – *Michelle Lane (Adelaide, Australia)*	**C.2 Parallel session** **Epigenetics, Diet and Metabolic Programming** *Hosts/Chairs: Richard Saffery, Marie-France Hivert* • Maternal hyper-glycaemia and fetal epigenetic adaptations – *Marie-France Hivert (Boston, USA)* • *High-fat diet during pregnancy and lactation alters DNA-methylation of key genes in lipid metabolism resulting in loss of protection from obesity in Gipr -/- mice offspring – Michael Kruse (Nuthetal, Germany)* • Intergenerational epigenetic inheritance in a murine model of undernutrition – *Elizabeth Radford (Cambridge, UK)* • *Genome-wide differential DNA methylation profiling of obese and lean teenagers in Finland – Trine Rounge (Oslo, Norway)* • Analysis of genome wide DNA methylation patterns to identify mechanisms of nutritional proramming – *Eva Reischl (Munich, Germany)*
19.00	**Welcome Reception (Alter Rathaussaal)**		

Friday, 14th March 2014

08.20 – 09.25	**Workshop (WS1): Body Composition Assessment in Mother-Offspring Studies** *Hosts/Chairs: Verónica Luque, Rebecca Moon* • Using peripheral quantitative computed tomography to assess bone and body composition *– Rebecca Moon (Southampton, UK)* • Air Displacement Plethysmography in infants and young children *– Stefanie Kouwenhoven (Amsterdam, The Netherlands)* - Lecture Hall II -	**Workshop (WS2): MedSciNet – Building an Electronic Data Capture System for a Clinical Trial** • Introduction to Electronic Data Capture systems *– Marius Kublickas* • Presentation *– Laima Juodvirsiene* - Study workflow – where to start, what to think about - Data validation - Data access levels - Data monitoring - Database lock and data download - Data interchange with other systems – possibilities, limitations • Discussion and questions *– Marius Kublickas, Laima Juodvirsiene, Magnus Westgren* - Lecture Hall III -	**Workshop (WS3): Sensitive Windows for Gene Environment Interactions in Early Life – Do They Matter?** *Host/Chair: Sylvain Sebert* • Early life drivers of the obesity epidemic ? *– Thorkild IA Sørensen (Copenhagen, Denmark)* • Nutrient-gene interaction in early life programming: two examples *– Eva Reischl (Munich, Germany)* • Impact of a diabetic intrauterine environment on childhood growth *– Sandra Hummel (Munich, Germany)* - Lecture Hall IV -
09.30 – 10.15 Lecture Hall III + IV	**Plenary Session III:** *Chair: Hans van Goudoever* **First Trimester Programming of Cardio-Metabolic Disease** – Vincent Jaddoe (Rotterdam, The Netherlands)		
10.15 – 10.45	***Coffee and Tea Break***		
10.45 – 12.20 **A.3:** Lecture Hall III **B.3:** Lecture Hall II **C.3:** Lecture Hall IV	**A.3 Parallel Session** **Increased Gestational Weight Gain vs. Pre-pregnancy Weight as Risk Factors for Childhood Adiposity** *Hosts: Julie Owens, Bernadeta Patro-Golab* *Chairs: Jodie Dodd, Bernadeta Patro-Golab* • Maternal vs. paternal body mass index and offspring obesity: A systematic review *– Bernadeta Patro-Golab (Warsaw, Poland)* • *Adherence to Mediterranean diet during pregnancy and childhood obesity at 4 years of age: Mother-child cohort study of Crete, Rhea study* *– Stella Koinaki (Heraklion, Greece)* • Should overweight or obese women be encouraged to lose weight to improve fetal growth? *– Andreas Beyerlein (Munich, Germany)*	**B.3 Parallel session** **Unpacking Complexity in Etiology and Implementation of Interventions** *Hosts/Chairs: Matt Gillman, Liz Considine* • Systems Science to Guide Implementation of Whole-of-community Childhood Obesity Interventions *– Matt Gillman (Boston, USA)* • *Type 2 Diabetes after exposure during gestation to the Ukraine Famine of 1933 – Lambert Lumey (New York, USA)* • Emerging genomics technologies in research of complex diseases – *André Uitterlinden (Rotterdam, The Netherlands)* • *Metabolic dysregulation in early pregnancy in association with offspring cardiometabolic risk in preschool children: The Mother Child "Rhea" Cohort in Crete, Greece* *– Vasiliki Daraki (Heraklion, Greece)*	**C.3 Parallel session** **Opportunities for Obesity Prevention in Early Childhood** *Hosts/Chairs: Joaquin Escribano, Manja Fleddermann* • Priming of the Obesity Risk by Smoking in Pregnancy *– Rüdiger von Kries (Munich, Germany)* • *Which costs does childhood obesity cause? Implications for obesity prevention in Germany* *– Freia de Bock (Mannheim, Germany)* • Complementary Feeding in Infancy *– Veit Grote (Munich, Germany)* • *Protein intake in early childhood is associated with obesity and cardiometabolic health at school age: The Generation R study* *– Trudy Voortman (Rotterdam, The Netherlands)*

Friday, 14th March 2014 (continued)

	• *Excessive maternal weight gain during gestation leads to offspring with increased adipogenic potential in the immediate perinatal period in pigs – Kolapo Ajuwon (West Lafayette, USA)* • Paternal factors and newborn size and adiposity – *Julie Owens (Adelaide, Australia)* – impact of an antenatal intervention to limit gestational weight gain	• Combining metabolomics and genetics data – a network approach – *Jan Krumsiek (Munich, Germany)*	• Nutritional challenges and opportunities during the weaning and toddler period – *Martine Alles (Danone, Utrecht, The Netherlands)*
12.20 – 13.25	***Lunch Break + Poster Viewing***	**12.30 – 13.30** **Industry sponsored Lunch Satellite Symposium:** **"Protein – Growth – Special needs"** • Influence of Maternal BMI and Protein in Infant Formulas on Growth of Infants – *Ferdinand Haschke (Nestlé, Vevey, Switzerland)* • Do all Preterm Infants need the same Amounts of Protein? – *Hans van Goudoever (Amsterdam, The Netherlands)* - Lecture Hall II -	**12.45 – 14.15** **DOHaD Society Annual Business Meeting (AGM)** - Lecture Hall III -
13.25 – 14.25	**Guided Poster Tour** I – Prevention and Intervention *Chair: Piotr Socha* II – Epidemiology *Chair: Vincent Jaddoe* III – Mechanisms *Chair: Michael Symonds*		
14.30 – 16.05 **A.4:** Lecture Hall III **B.4:** Lecture Hall II **C.4:** Lecture Hall IV	**A.4 Parallel Session** **Mechanistic Insights from Animal Studies (Chair: Ricardo Rueda)** *Hosts/Chairs: Sue Ozanne, Denise Fernandez-Twinn* • Programming by maternal diet-induced obesity - mechanistic insights for intervention strategies – *Susan Ozanne (Cambridge, UK)* • *Perinatal nutritional programming of adipose tissue inflammation and metabolic dysfunction in diet-induced obesity – Brandon Kayser (Los Angeles, USA)* • Mechanisms underlying programming by maternal obesity - the power of large animal models – *Peter Nathanielsz (Texas, USA)*	**B.4 Parallel session** **Breast Feeding and Breast Milk Components - What is Important for Short and Long Term Development?** *Hosts/Chairs: Wendy Oddy, Hans Demmelmair* • A longitudinal cohort study to investigate associations between infant feeding and overweight into the adult years – *Wendy Oddy (Perth, Australia)* • *Exclusive breastfeeding duration and cardiorespiratory fitness in children and adolescents – Jonatan Ruiz (Granada, Spain)* • Lactation and intergenerational health of mothers and children – *Matt Gillman (Boston, USA)*	**C.4 Parallel session** **The Role of Endocrine Regulation (Including Letin / Igfs) in Fetal and Postnatal Adiposity** *Hosts/Chairs: Gernot Desoye, Paul Taylor* • Maternal obesity and the developmental programming of offspring appetite and obesity: A role for leptin? – *Paul Taylor (London, UK)* • *Changes in neonatal nutrition modify hypothalamic leptin responsiveness in adult life – Paula Marangon (Ribeirao Preto, Brazil)* • Growth factors and their role in adipose tissue development in early life – *Mike Symonds (Nottingham, UK)*

	• *Early supplementation of non-obese diabetic mice with oligosaccharides isolated from human milk reduces spontaneous autoimmune diabetes development later in life – Gert Folkerts (Utrecht, The Netherlands)* • Role of feeding with slow digesting carbohydrates during pregnancy on improving metabolic health in the offspring: Mechanistic insights – *Jose-Maria Lopez Pedrosa (Abbott, Granada, Spain)*	• *Growth, nutrition and early programming of immune function in breast-fed infants and infants fed formula with added osteopontin (OPN) – Bo Lönnerdal (California, USA)* • Breast milk and growth – *Maria Grunewald (Munich, Germany)*	• *Molecular mechanisms of renal dysfunction and hypertension secondary to neonatal hyperleptinaemia – Anne-Maj Samuelsson (London, UK)* • Endocrine programming of hypothalamic feeding circuits – *Sebastien Bouret (Los Angeles, USA)*
16.05 – 16.30	***Coffee and Tea Break***		
16.30 – 18.05 **A.5:** Lecture Hall III **B.5:** Lecture Hall II **C.5:** Lecture Hall IV	**A.5 Parallel session** **The Role of Infant Feeding** *Hosts/Chairs: Hans van Goudoever, Bartlomiej Zalewski* • Qualitative developments in infant feeding – lessons from animal models – *Per Sangild (Copenhagen, Denmark)* • *Impact of nutrient density of formula on nutritional intakes in healthy term infants and the influence of home reconstitution – Jacques Rigo (Liege, Belgium)* • Effects of protein supply on child growth and body composition – *Martina Weber (Munich, Germany)* • *Iron and vitamin D deficiency in preterm babies – a potential programming link to cardiovascular disease in later life – Cathryn Conlon (Auckland, New Zealand)* • Energetic efficiency of infant formulae – *Manja Fleddermann (Munich, Germany)*	**B.5 Parallel session** **The Toxic Environment and Perinatal Programming of Obesity and Dysmetabolism** *Hosts: Emily Oken, Merete Eggesbø* *Chairs: Rüdiger von Kries, Emily Oken* • Prenatal air pollution exposure, later growth and cardio-metabolic risk – *Emily Oken (Boston, USA)* • *Associations of in-utero smoke exposure and breastfeeding behavior with later autonomic nervous system function at preschool-age - preliminary evidence for "autonomic programming"? – Freia De Bock (Mannheim, Germany)* • Prenatal exposures to persistent organohalogen contaminants in relation to offspring adiposity and cardio-metabolic risk factors at 20 years of age – *Thorhallur Halldorsson (Copenhagen, Denmark)* • *Organic food consumption and the risk of preeclampsia; results from the Norwegian Mother and Child Cohort Study – Hanne Torjusen (Oslo, Norway)* • Infants under double attack? The role of environmental toxicants and gut microbiota in rapid growth and childhood obesity – *Merete Eggesbø (Oslo, Norway)*	**C.5 Parallel Session** **Recommendations for Practice** *Hosts/Chairs: Hania Szajewska, Stefanie Kouwenhoven* • Guidelines, recommendations, etc. – Based on eminence or evidence? – *Hania Szajewska (Warsaw, Poland)* • *How can vulnerable people be reached to reduce adverse health-related perinatal programming effects? – Helena Walz (Fulda, Germany)* • The Southampton Women's Survey: from observational evidence to behavior change interventions. – *Hazel Inskip (Southampton, UK)* • *Ludical activities, facebook interaction and instant messages for children with cardiovascular risk factors impacts both children and caregivers: A randomized clinical trial – Lucia Pellanda (Porto Alegre, Brazil)* • Nutrition research and food legislation - the role of EFSA – *Hildegard Przyrembel (Berlin, Germany)*
19.30	**Conference Dinner: Bavarian Evening (Hofbräukeller)** **Dinner Debate: "Special guests invited: Charles Darwin and Jean-Baptiste Lamarck"**		

Saturday, 15th March 2014

09.00 – 10.05 — Breakfast Symposia

I.Family: Health and development of small children: Observations from the IDEFICS-I.Family Cohort

Host/Chair: Wolfgang Ahrens

- Pre- and perinatal influences on the weight status of primary school children – *Wolfgang Ahrens (Bremen Germany), Alfonso Siani (Avellino, Italy)*
- Ethical issues in large-cohort research: social relevance and distributed responsibilities – *Garrath Williams (Lancaster, UK)*
- Expected future insights from the I.Family Study – *Iris Pigeot (Bremen, Germany), Wolfgang Ahrens (Bremen, Germany)*

- Lecture Hall II -

Horizon 2020: EU Research and Innovation Programme

Host/Chair: Isabelle de Froidmont-Görtz, European Commission, DG Research and Innovation

- Horizon 2020: Research opportunities in the food sector for a safe and healthy diet – *Isabelle de Froidmont-Görtz (Brussels, Belgium)*
- Grant application: Some tips – *Berthold Koletzko (Munich, Germany)*
- Coordinator experiences – *Cristina Campoy (Granada, Spain)*

- Lecture Hall IV -

New Investigators Forum

Hosts/Chairs: Stefanie Kouwenhoven, Olaf Uhl

- Finding spontaneous preterm birth biomarkers from metabolomics data when unknown subgroups exist – *Liz Considine (Cork, Ireland)*
- The Young Coeliacs of the PreventCD Study – A Prospective Cohort at High-Risk for Coeliac Disease – *Sabine Vriezinga (Leiden, The Netherlands)*
- Metabolite profiling of blood plasma in the field of early nutrition – *Olaf Uhl (Munich, Germany)*
- Maternal intake of vitamin A in mid-pregnancy and risk of child asthma – *Ekaterina Maslova (Copenhagen, Denmark)*

- Lecture Hall III -

10.10 – 11.45

A.6: Lecture Hall III

B.6: Lecture Hall II

C.6: Lecture Hall IV

A.6 Parallel session

Early Child Growth Trajectories as a Predictor of Childhood Obesity

Hosts/Chairs: Peter Rzehak, Romy Gaillard

- Importance of characterizing growth trajectories – *Matt Gillman (Boston, USA)*
- *The effect of antenatal dietary and lifestyle advice on fetal growth in women who are overweight or obese: findings from the LIMIT randomised trial – Rosalie Grivell (Adelaide, Australia)*
- Metabolic markers, rapid growth and obesity at age 6 years – *Peter Rzehak (Munich, Germany)*
- *Maternal 25-hydroxy-vitamin D status in late pregnancy and offspring muscle development: Findings from the Southampton Women´s Survey (SWS) – Rebecca Moon (Southampton, UK)*
- Cord blood biomarkers of the fetal metabolism: associations with postnatal growth and later metabolism – *Nolwenn Regnault (Paris, France)*

B.6 Parallel Session

Physical Activity in Pregnancy

Hosts/Chairs: Sjurdur Frodi Olsen, Julia Birnbaum

- UPBEAT study: Association between physical activity in obese pregnant women and health of the offspring – *Louise Hayes (Newcastle, UK)*
- *Exercise before and during an obese mouse pregnancy restores maternal glucose tolerance – Denise Fernandez-Twinn (Cambridge, UK)*
- Physical activity before and during pregnancy and birth weight – *Katrine Owe (Oslo, Norway)*
- *Maternal physical activity before and during pregnancy and offspring adiposity at mid-childhood – Kai Ling Kong (Buffalo, USA)*
- Physical activity in pregnancy and risk of gestational diabetes – *Marin Strøm (Copenhagen, Denmark)*

C.6 Parallel session

The Contribution of Public Private Collaboration (PPC) to Translational Research

Hosts: Eline van der Beek, Ricardo Rueda

Chairs: Silke Mader, Ricardo Uauy

- PPC: Benefits, challenges and risks from the perspective of Academia – *Mark Hanson (Southampton, UK)*
- Driving science that matters through PPC: examples of collaboration – *Ricardo Rueda (Abbott, Spain)*
- Public-private partnership insights from preclinical and epidemiological studies: tools to shape nutritional intervention trials – *Eline van der Beek (Danone, Singapore)*

11.45 – 12.05	***Coffee and Tea Break***		
12.05 – 12.50 Lecture Hall III + IV	**Plenary Session IV** *Chair: Sjurdur Frodi Olsen* **Insights from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) Cohort Study –** Keith Godfrey (Southampton, UK)		
12.50 – 13.35 Lecture Hall III + IV	**Closing Session** **Assessing Impact of Early Life Interventions –** Ricardo Uauy (Santiago, Chile) **Presentation of New Investigator Awards and Farewell Note** – Berthold Koletzko (Munich, Germany)		
13.35 – 14.00	***Farewell Snack***		
14.30 – 18.00 Lecture Hall IV	**Industry sponsored Satellite Symposium: "Meeting Nutrient Needs in the first 1,000 days of Life"** • Multiple micronutrient supplementation during pregnancy and lactation in low developing country settings: Impact on pregnancy outcomes (separate registration necessary(*– Zulfiquar A. Bhutta (Karachi, Pakistan)* • Multiple micronutrient needs in pregnancy and lactation in industrialized countries *– Irene Cetin (Milan, Italy)* • The role of long-chain polyunsaturated fatty acids in pregnancy, lactation and infancy *– Berthold Koletzko (Munich, Germany)* • Gaps in meeting nutrient needs in healthy toddlers *– Tamas Decsi (Pecs, Hungary)* • Quality and safety aspects of ingredients for supplements and food products addressing pregnant women and infants *– Manfred Eggersdorfer (DSM, Basel, Switzerland)* • Roundtable discussion		

THE POWER OF PROGRAMMING
International Conference on Developmental Origins of Adiposity and Long-Term Health
March 13 - 15, 2014, University Hospital of Munich, Campus Grosshadern

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COSMED	1
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Nestlé	4
European Foundation for the Care of Newborn Infants (EFCNI)	5

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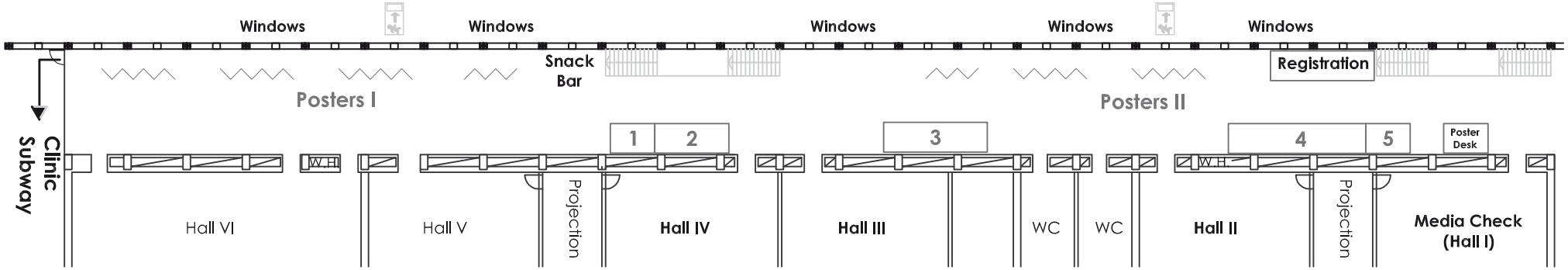

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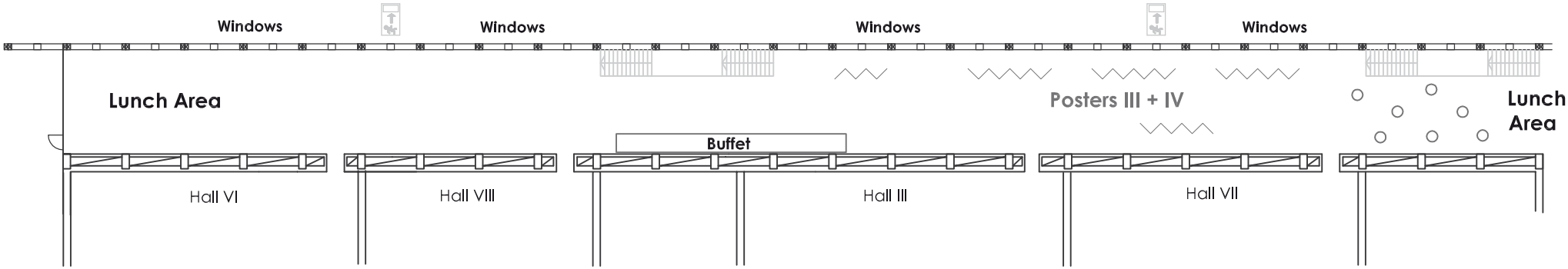

As of February 12, 2014. The floor plan is subject to changes.

page

PLENARY SESSIONS

I. The LIMIT Randomized Trial

EARLYNUTRITIONMEMBER

Thursday 13th March, 10.45-11.30

Dodd JM, Turnbull D, McPhee AJ, Deussen AR, Grivell RM, Yelland LN, Crowther CA, Wittert G, Owens JA, Robinson JS

Discipline of Obstetrics & Gynaecology, and the Robinson Institute, The University of Adelaide, ADELAIDE, SOUTH AUSTRALIA

Overweight and obesity during pregnancy is common. Robust evidence about the effect of antenatal dietary and lifestyle interventions on health outcomes is lacking.
We conducted a multicentre, randomised trial, recruiting 2,212 women from three public maternity hospitals across South Australia, with a singleton pregnancy, between 10^{+0} and 20^{+0} weeks gestation, and body mass index (BMI) >25kg/m^2. Women were randomised to Lifestyle Advice (n=1,108) or Standard Care (n=1,104).
Women randomised to Lifestyle Advice participated in a comprehensive dietary and lifestyle intervention over pregnancy, delivered by research staff.
Women randomised to Standard Care received pregnancy care according to local guidelines, which did not include such information.
Infants born to women following lifestyle advice were significantly less likely to have birth weight above 4.0kg (aRR 0.82; 95% CI 0.68 to 0.99; p=0.04), or above 4·5kg (aRR 0·59; 95% CI 0·36-0·98; p=0·04). There were no differences identified in maternal pregnancy and birth outcomes between the two treatment groups.
For women who are overweight or obese, antenatal lifestyle advice improves maternal diet quality, and significantly reduces the risk of infant birth weight above 4kg. It will be important to continue to follow-up the infants born to women in this trial.

II. Epigenetics as the Major Mediator of Fetal Programming: Are We There Yet?

EARLYNUTRITIONMEMBER

Thursday 13th March, 15.00-15.45

Richard Saffery

Murdoch Children's Research Institute and University of Melbourne, MELBOURNE, AUSTRALIA

Barker and colleagues were the first to highlight the potential for the in utero environment to influence later adult health by identifying a negative association between death from cardiovascular-related disease and birth weight [1]. This initial observation was subsequently expanded to the Developmental Origins of Health and Disease (DOHaD) hypothesis, supported by a large number of studies in animals and fewer, largely observational, studies in humans. In utero epigenetic variation has emerged as a prime candidate as the mediator of such long term 'programming' effects, yet despite compelling reports from animal models and observational studies in humans, the field suffers from a general lack of replication and over interpretation of findings. Nevertheless, amongst the flood of publication 'noise' in this growing field, some key findings are emerging, particularly in relation to smoking as a driver of specific and stable epigenetic change in humans.
Prerequisites for establishing a causal link include; (i) demonstrating inter-individual epigenetic variability in early life (including at birth), (ii) in response to specific environmental exposures and/or (iii) genetic factors. Further, (iv) compelling evidence linking epigenetic change to disease, prior to onset is required. Finally, (v) the functional relevance of specific epigenetic change must be demonstrated. Ultimately, only large longitudinal life-course studies, commencing prior to birth, can provide direct evidence in support of a role of epigenetics as a driver of DOHaD, but these will take decades to mature. Nevertheless, recent data are promising and provide confidence that epigenetic processes underpin at least part of the DOHaD causal pathway associated with the developing 'epidemic' of non-communicable diseases in the 21st century.

[1] Barker DJ, Bull AR, Osmond C, Simmonds SJ: Fetal and placental size and risk of hypertension in adult life. BMJ 1990, 301:259-62.

III. First Trimester Programming of Cardio-Metabolic Disease

EARLYNUTRITIONMEMBER

Friday 14th March, 9.30-10.15

Vincent W.V Jaddoe

Department of Paediatrics, Department of Epidemiology, Erasmus University Medical Center, Sophia Children's Hospital, ROTTERDAM, THE NETHERLANDS

Both a low and high birth weight are associated with type 2 diabetes in adulthood. Clearly, birth weight is not the causal factor per se leading to type 2 diabetes in later life. A specific birth weight is the result of different adverse exposures and growth patterns in fetal life and is the point of departure for childhood growth variation. Studies focused on specific growth patterns; critical periods for specific adverse exposures; and the role of (epi) genetic variation may help to elucidate the underlying mechanisms. First, both individuals with a high birth weight and individuals with a low birth weight followed by an early catch up growth are at increased risk of overweight and type 2 diabetes in later life. Second, an accumulating body of evidence suggest that adverse maternal life-style related habits such as maternal obesity and smoking during pregnancy influence both growth patterns in fetal life and infancy and body fat distribution in childhood. Recent studies suggest that these adverse exposures also lead to increased risks of obesity and type 2 diabetes in adulthood. Third, the associations of birth weight with type 2 diabetes may also be explained by common genetic variants involved in glucose and insulin metabolism. Prospective cohort study designs, with detailed environmental exposure, genetic and follow-up data, and advanced approaches to deal with confounders will help to identify early life exposures and growth patterns leading to obesity and type 2 diabetes in later life.

IV. Insights from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) Cohort Study

EARLYNUTRITIONMEMBER

Saturday 15th March, 12.05-12.50

Godfrey KM [1,2], Soh SE [2], Meaney M [3], Gluckman PD [3,4], Chong YS [2,3], GUSTO Study Group

[1] Medical Research Council Lifecourse Epidemiology Unit & NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, SOUTHAMPTON, UK;

[2] National University of Singapore, SINGAPORE

[3] Singapore Institute for Clinical Sciences, A'STAR, SINGAPORE;

[4] Liggins Institute, University of Auckland, AUCKLAND, NEW ZEALAND

The dramatic emergence of non-communicable diseases in Asia, albeit with ethnic variation, has coincided with the rapid socioeconomic and nutritional transition taking place in the region, with the prevalence of diabetes rising five-fold in Singapore in less than four decades. The Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort study recruited 1247 expectant mothers of Chinese, Malay or Indian ethnicities in their first trimester (June 2009 to September 2010) with detailed longitudinal tracking - through the antenatal period, birth and the child's first 4 years of life to examine the potential roles of fetal, developmental and epigenetic factors in early pathways to obesity and metabolic compromise.[1] Follow up of mother and child after 4 years is in plan. Beyond the core focus on metabolic disease, the richness of the clinical data of three distinct ethnicities, the extent of biological sample collection and the extensive follow up in the early years of life has allowed us to investigate other outcomes, in particular, neurocognitive, behavioural, ocular and allergic outcomes. We have found a higher incidence of gestational diabetes mellitus (GDM) in Indians and Chinese than previously suspected, and that higher glucose levels in mother even in the absence of GDM, affect infant adiposity. Ethnic differences in body composition were observed at birth, with Indian and Malay infants having greater abdominal superficial and deep subcutaneous tissues, but smaller internal adipose tissue depots than Chinese infants. Brain morphological shape and white matter microstructure differences were observed using neonatal MRI and diffusion tensor imaging.

1. Soh SE, Tint MT, Gluckman PD, Godfrey KM, Rifkin-Graboi A, Chan YH, Stünkel W, Holbrook JD, Kwek K, Chong YS, Saw SM; the GUSTO Study Group. Cohort Profile: Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort study. Int J Epidemiol 2013 – epub Sep 25.

Closing Session:

Assessing Impact of Early Life Interventions

Saturday 15th March, 12.50-13.35

Ricardo Uauy [1-3]

[1] Institute of Nutrition University of Chile. INTA University of Chile, SANTIAGO, CHILE

[2] Department of Pediatrics. Catholic University of Chile, SANTIAGO, CHILE

[3] London School of Hygiene and Tropical Medicine, LONDON, UK.

Early life interventions to prevent the consequences of malnutrition are now well established as a priority for global health and human development. The prevention of early death is a key component of the millennium development goals to be met by 2015. We now promote optimal growth and mental development as key for human-social development; the early years lay the biological foundation for productive social and educational investments, building human capital with lifelong returns. We recognize that the interventions required to prevent stunting and improve brain development are complementary but differ from those needed to reduce underweight & wasting. The issue is not about choosing between addressing under-nutrition in the poor versus treating obesity in the affluent; but how to maximize human development potential preventing death/disability in the early years with a life course perspective. We need to assess the biological, social and economic impact of the various options beyond counting lives saved; we must include the quality of life of those lives and the economic benefits to individuals and society. The economic cost of preventable "adult non communicable chronic diseases" (NCDs) must be integrated in our impact analysis of early nutrition interventions. The largest fraction of these losses relate to poorer brain development and lower educational achievement followed by early death/disability of adults, all impact economic productivity and national development.

Parallel Sessions

A.1: Glycaemic Load in Pregnancy – Opportunities for Prevention?

Thursday 13th March, 11.50-13.25

The UPBEAT study: A lifestyle intervention in obese pregnant women

EARLYNUTRITIONMEMBER

Lucilla Poston
Division of Women's Health, Women's Health Academic Centre, King's College London, LONDON, UK

Observational studies report an independent relationship between maternal obesity and adiposity in the child in later life, but the relative role played by the environment in utero and other known determinants of childhood obesity remains unknown. Intervention studies to improve pregnancy outcome in obese women may provide insight. To date, lifestyle interventions have met with limited success in improving maternal and neonatal outcomes, likely at least in part to be due to barriers to behavioural change. It is important that lifestyle interventions should be known to change behaviour before embarking on large clinical trials. UPBEAT is a randomized controlled trial of 1546 obese pregnant women randomized to standard antenatal care or to a health trainer led intervention (low glycemic index, low saturated fat, reduced free sugars; increased physical activity). The primary outcome for the mother is GDM and for the infant, macrosomia. Childhood adiposity is a secondary outcome. A pilot study showed the intervention reduced the dietary glycemic load by 25% and saturated fat by 13%, as well as changing, in a 'healthy' direction two of three identified food patterns. These changes probably reflect intervention intensity; (8 weekly sessions, with weekly goal setting). UPBEAT will report maternal and clinical outcomes in 2014. Over the next three years, as part of the EarlyNutrition EU programme, measures of adiposity, diet, physical activity and cardiovascular function will be determined in 3yr old UPBEAT children. The UPBEAT biobank will be utilized to assess mechanistic pathways underlying the relationships between maternal and child obesity.

A pilot study to evaluate the effects of a dietary supplement with slow digesting-low GI carbohydrates in obese pregnant women using continuous glucose monitoring

EARLYNUTRITIONMEMBER

Maitland R.A. [1], Patel N. [1], Sherry C. [2], Marriage B. [2], Barr S. [1], Lopez J.M. [3], Murphy H. [4], Thomas S. [5], Fernández L.G. [6], Rueda R. [3], Poston L. [1]
[1] King's College London, Women's Health Academic Centre, King's Health Partners, LONDON, UNITED KINGDOM
[2] Abbott Nutrition, Paediatric Research & Development, COLUMBUS, UNITED STATES
[3] Abbott Nutrition, Discovery: Research and Development, GRANADA, SPAIN
[4] University of Cambridge, Department of Clinical Biochemistry, CAMBRIDGE, UNITED KINGDOM
[5] Guy's and St.Thomas' NHS Foundation Trust, Diabetes and Endocrinology, LONDON, UNITED KINGDOM
[6] Seplin Statistical Solutions, GRANADA, SPAIN

Background: Obesity in pregnancy is associated with higher postprandial glycaemic response (PGR), insulin resistance and macrosomia. Dietary supplements with slow digesting-low GI carbohydrates (SD-LGI) may blunt the PGR, contributing to improved glucose homeostasis and reduced risk of adverse outcomes.
Aim: To investigate effects of a SD-LGI supplement compared to a control supplement with rapidly digesting carbohydrates in obese pregnant women.
Study design: Sixteen obese, pregnant women (24+0-28+6 gestation) participated in a cross-over, randomized study. The control or test supplement was taken with breakfast and an afternoon snack for a 2-day period (hospital [day-1] and home [day-2]). Following a 2-day washout period the protocol was repeated with the alternative supplement. 24hr blood glucose was monitored throughout (Abbott FreeStyle Navigator® continuous glucose monitor sensor).
Results: Preliminary mixed model regression analysis (n=16; BMI 36.58, SE 1.16) demonstrated higher estimates of the main effect for daytime-glucose over the 2-day period in control vs. treatment (0.258, SE 0.042, p< 0.001 [95%CI 0.176-0.341]). Significant changes of the effect by hospital and period were found with no nighttime differences observed. PGR for all meals consumed on day-1, but not day-2, was lower in women taking the test supplement (change of the effect day-1: breakfast 0.181, SE 0.066, p=0.007 [95%CI 0.05-0.311]; lunch 0.637, SE 0.295, p=0.038 [95%CI 0.039-1.235]; dinner 0.421, SE 0.081, p< 0.001 [95%CI 0.263-0.580]).
Conclusions: The SD-LGI supplement reduced daytime glucose in obese pregnant women. A supplement containing SD-LGI carbohydrates with food may offer an approach to improving glucose homeostasis in obese pregnant women.

Dietary and physical activity interventions for women who are overweight or obese during pregnancy – the findings of the LIMIT randomized trial

EARLYNUTRITIONMEMBER

Dodd JM, Turnbull D, McPhee AJ, Deussen AR, Grivell RM, Yelland LN, Crowther CA, Wittert G, Owens JA, Robinson JS
Discipline of Obstetrics & Gynaecology, and the Robinson Institute, The University of Adelaide, ADELAIDE, AUSTRALIA

Overweight and obesity during pregnancy is common. However, there is little evidence in the literature describing dietary and physical activity changes following interventions during pregnancy.
We conducted a multicentre, randomised trial, recruiting 2,212 women from three public maternity hospitals across South Australia, with a singleton pregnancy, between 10+0 and 20+0 weeks gestation, and body mass index (BMI) >25kg/m2. Women were randomised to Lifestyle Advice (n=1,108) or Standard Care (n=1,104).
Women randomised to Lifestyle Advice participated in a comprehensive dietary and lifestyle intervention over pregnancy, delivered by research staff. Women were provided with dietary advice consistent with current Australian standards, to maintain a balance of carbohydrates, fat and protein, to reduce intake of foods high in refined carbohydrates and saturated fats, while increasing intake of fibre, and promoting consumption of two serves of fruit, five serves of vegetables, and three serves of dairy each day. Physical activity advice

primarily encouraged women to increase their amount of walking and incidental activity.
Women randomised to Standard Care received pregnancy care according to local guidelines, which did not include such information. Women who received Lifestyle Advice improved their diet quality, significantly increasing consumption of protein (p=0.03), fibre (p=0.001), fruits (p=0.003) and vegetables (p=0.003), decreasing energy from total fat (p=0.02) and saturated fat (p=0.007), and increasing household related physical activity (p=0.008). However gestational weight gain did not differ. For women who are overweight or obese, antenatal lifestyle advice improves maternal diet quality and physical activity during pregnancy.

Maternal and fetal predictors for the therapy-management by gestational diabetes

Groten T. [1], Schneider S. [1], Schleußner E. [1], Battefeld W. [2]
Universitätsklinikum Jena, [1] Geburtshilfe, [2] Klinik für Innere Medizin III, JENA, GERMANY

Background: German guidelines in treatment of diabetes in pregnancy implicate fetal growth parameters in the decision when to start an insulin therapy. However, growth parameters demonstrating abnormal abdominal growth already reflect fetal hyperinsuliniemia which might have been prevented by earlier intervention. The goal of this study was to define maternal and fetal markers predicting the necessity of insulin therapy.
Methods: In a hospital based prospective cohort study 255 patients were tested for gestational diabetes. In 135 cases were a gestational diabetes fetal and maternal parameters were analysed in relation to the need of insulin therapy.
Results: In 44% of pregnant women with gestational diabetes insulin therapy was necessary. In 14% (n=8) of GDM cases treated with insulin therapy where started due to abnormal fetal growth parameters. Multiple logistic regression analysis revealed thickness of fetal abdominal skin layer of more than 4 mm and fetal weight > 75. Percentile, maternal age > 30 years, history of gestational diabetes, BMI > 25 before pregnancy and HbA1c > 5.2% at the time of diagnosis were predictive for the need of insulin therapy. The positive predictive value for the fetal parameters alone was 62.7%, for the maternal parameter 71.5% and in combination 77.6%.
Conclusions: Our data support the concept that maternal and fetal parameters already at the time of diagnosis predict the need of insulin therapy. We conclude that in the presence of these parameters the time of starting insulin therapy in patients with gestational diabetes could be optimized.

Maternal nutrition and fetal health

EARLYNUTRITIONMEMBER

Fionnuala McAuliffe
University College Dublin, School of Medicine and Medical Science, DUBLIN, IRELAND

Worldwide obesity rates have almost doubled since 1980. In recent years the escalating rate of childhood obesity in particular has emerged as a significant public health concern. It is well established that obesity in childhood increases the risk of obesity in adulthood and infants that are large for gestational age at birth are more likely to be obese in childhood. Pregnancy, therefore, is a critical period during which fetal programming occurs that dictates later childhood and adult health. It remains a potentially preventable "illness" and is one which we urgently need to understand.
Maternal glucose homeostasis is intrinsically linked to intrauterine growth and maternal hyperglycaemia, even at levels below those diagnostic of diabetes and predisposes to fetal macrosomia and adverse obstetric outcomes.
The ROLO study published in 2012 was a large randomised control trial of low glycaemic index diet in pregnancy to prevent the recurrence of macrosomia. Despite demonstrating a significant reduction in glycaemic index in the intervention group the ROLO study found that a low glycaemic index diet in pregnancy has no impact on infant birthweight in a group of women at risk of fetal macrosomia. It does, however, have a significant positive effect on two important maternal outcomes, gestational weight gain and glucose intolerance. Additionally neonates whose mothers had a low GI diet in pregnancy had lower thigh circumference. These findings suggest that maternal low GI diet is safe in pregnancy and may positively impact both maternal health and infant adiposity.

B.1: Metabolic Predictors of Maternal and Childhood Obesity

Thursday 13th March 11.50 – 13.25

Fatty acid composition in blood and obesity in childhood

Marie Standl
Institute of Epidemiology I, Helmholtz Zentrum München – German Research Centre for Environmental Health, NEUHERBERG, GERMANY.

An increased intake of n-6 polyunsaturated fatty acids (PUFAs), which yields a higher n-6 to n-3 PUFA ratio, has been suggested to promote adipose tissue development. Cross-sectional studies suggest that obese subjects have lower concentrations of n-3 long-chain (LC-) PUFAs in blood. In order to improve the n-3 LC-PUFA supply and thereby prevent obesity, intervention studies have mainly focused on pregnant or breastfeeding women, as the pre- and early postnatal life are critical periods for adipose tissue development. To date, despite a biologically plausible mechanism, observational and intervention studies have failed to provide a consistent picture of the association between LC-PUFA concentrations in early life and weight development. Observational studies report negative associations between maternal n-6 LC-PUFA status and childhood obesity or fat mass. Intervention studies on this association have yielded inconsistent results, especially for studies with repeated follow-ups and several endpoints. Published reviews and meta-analyses have also failed to provide a consistent picture. Recently, published studies have suggested that it might be more efficient to reduce the n-6/n-3 PUFA ratio by not only increasing n-3 LC-PUFA concentrations but also by reducing n-6 LC-PUFA concentrations. It has also been suggested that the effect of LC-PUFAs in early life on later BMI might change over time. More longitudinal studies with adequate sample sizes and repeated measurements are needed to fully assess the long-term effect of LC-PUFAs in early life on body composition and weight development. Only with additional studies will we be able to develop evidence-based dietary recommendations during pregnancy.

Metabolomic profiles of childhood obesity

☆ *New Investigator Award*

Perng W. [1], Gillman M.W. [1,2], Fleisch A.F. [3], Michalek R. [4], Watkins S. [4], Patti M.-E. [5], Oken E. [1]

[1] Harvard Medical School and Harvard Pilgrim Health Care Institute, Population Medicine, BOSTON, UNITED STATES

[2] Harvard School of Public Health, Department of Nutrition, BOSTON, UNITED STATES

[3] Boston Children's Hospital, BOSTON, UNITED STATES

[4] Lipomics, A Division of Metabolon Inc., WEST SACRAMENTO, UNITED STATES

[5] Joslin Diabetes Center, BOSTON, UNITED STATES

Objective: To identify metabolite patterns associated with obesity and cardiometabolic risk during midchildhood, and to evaluate the extent to which maternal peripartum factors influence offspring metabolite profiles.

Methods: We quantified 345 metabolites in serum of 262 children 7-10 years and consolidated them into 18 patterns using principal components analysis. We compared factor scores for each pattern between obese (BMI≥95%tile; ***n***=84) and lean children (BMI< 85%tile; ***n***=150). Two patterns were associated with obesity: a branched-chain amino acid (BCAA)-related pattern and a steroid hormone pattern composed of androgen precursors. Using multivariable linear regression models that adjusted for maternal education, child´s age, sex, race, and fast-food intake, we examined relations of the metabolite patterns with HOMA-IR, leptin, CRP, and IL-6. We also investigated associations of maternal pre-pregnancy obesity, excessive gestational weight gain, and gestational glucose tolerance with the metabolite patterns.

Results: After adjustment for confounders, the BCAA and steroid patterns were both directly related to the cardiometabolic biomarkers. For example, each increment in both the BCAA and the steroid score corresponded with 6% (1%, 13%) higher HOMA-IR, respectively. Children of obese mothers had 0.65 (0.18, 1.11) higher BCAA score than their counterparts. This association was somewhat attenuated after adjustment for father´s BMI, breastfeeding duration, and child´s fast-food intake (0.48 [-0.05, 1.02]). None of the other maternal characteristics were related to either metabolite pattern.

Conclusions: Disturbances in BCAA catabolism and elevated steroid hormones are associated with obesity and cardiometabolic risk during mid-childhood. Maternal obesity may contribute to alterations in offspring BCAA metabolism.

Influence of early nutrition on metabolic processes – Investigated by targeted LC/MS based metabolomics

EARLYNUTRITIONMEMBER

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Pre- and postnatal nutrition can program later metabolic response and disease risks. Breastfeeding and longer duration of breastfeeding are considered to have beneficial effects on growth. The underlying mechanisms remain unclear. Metabolic analyses offer opportunities to enhance the understanding of metabolic regulation in response to environmental influences. Insights are possible at the molecular level by determining up- and down-regulations of metabolic pathway activities. We established a targeted metabolomics platform that is used within the collaborative research project "EarlyNutrition". The platform facilitates an accurate quantification of known lipid metabolites and amino acids. For instance, the platform has been applied to blood plasma samples from children participating in the randomized controlled Childhood Obesity Project Trial. During the first year of life they received infant and follow-on formulae with higher or lower protein contents but equal energy density, while a reference group was breastfed. Children with higher protein intakes showed increased plasma concentrations of branched-chain amino acids (BCAA) and their related oxidation products, short-chain acylcarnitines, compared to those with lower protein intakes and those who were breastfed. This indicates alterations in the BCAA metabolism. Metabolic predictors of different growth patterns will be explored. We plan to investigate the influence of further variables such as prenatal maternal psychosocial stress, nutrition during pregnancy, placental dysfunction, and variation in breast milk composition on maternal and/or infantile metabolic response in further studies within the "EarlyNutrition" collaboration.

Acknowledgement: Work reported herein is carried out with partial financial support from the Commission of the European Communities, the 7th Framework Programme, contract FP7-289346-EARLY NUTRITION and the European Research Council Advanced Grant ERC-2012-AdG – no.322605 META-GROWTH. This manuscript does not necessarily reflect the views of the Commission and in no way anticipates the future policy in this area. Additional support was received from the National Competence Network on Obesity, Grant Nr. 01 GI 0825, German Ministry of Education and Research, Berlin.

Evaluation of ursodeoxycholic acid (UDCA) to ameliorate maternal cholestasis-induced metabolic abnormalities in the fetus and offspring

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Background: The intrauterine environment is a major contributor to increased rates of metabolic disease in adults. Intrahepatic cholestasis of pregnancy (ICP) is a liver disease of pregnancy that is characterised by increased maternal bile acid (BA) levels and dyslipidaemia. It affects 0.5-2% of pregnant women. We recently established in human and mouse that cholestatic pregnancy has an impact on the metabolic health of the offspring and this is triggered by metabolic abnormalities in the fetoplacental unit. We hypothesised that ursodeoxycholic acid (UDCA), the drug that is used to treat ICP, can ameliorate the abnormal phenotype of the fetoplacental unit and potentially the metabolic health of the offspring of affected pregnancies.

Methods: BA-fed mice (cholestatic mice) were supplemented with UDCA during pregnancy. Maternal liver, placenta and fetal liver were

collected on the day 18 of pregnancy and gene expression was evaluated using real-time PCR.
Results: UDCA improved the cholestatic phenotype in the mother via down-regulation of BA-induced Shp, Bsep and Mrp-2 mRNA levels in the liver. Moreover, UDCA partially ameliorated maternal dyslipidaemia as it downregulated the cholesterol and triglyceride synthesis genes, Hmgcr and Fas. Similarly, UDCA improved BAinduced Hmgcr and Fas in the fetal liver. Ongoing studies will characterise the effects of UDCA on the placenta lipid homeostasis.
Discussion: We have shown that UDCA improves maternal cholestasis, dyslipidaemia and also fetal abnormal lipid metabolism. It is yet to be studied whether intervention with UDCA can reverse the abnormal metabolic phenotype later in life of the offspring as well.

Metabolic pathways to diabetes and obesity

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Primary obesity is associated with several cardiometabolic co-morbidities including non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes. However, the specific underlying mechanisms linking the expansion of adipose tissue to these co-morbidities are unknown. In our research we found that acquired obesity is associated with remodeling of membrane lipids in the adipose tissue. The remodeling may help maintain biophysical properties of lipid membranes, however at the cost of increased vulnerability to inflammation. We also found that the lipid molecular network behind the membrane lipid remodeling is amenable to genetic manipulation. In another study, we identified and validated a serum lipid signature which can be used in the estimation of liver fat and diagnosis of NAFLD, and is also predictive of type 2 diabetes. In another study, we applied the genome-scale human metabolic model and integrated it with two independent human experimental settings to study NAFLD. We identified a systemic shift of liver metabolism in NAFLD towards reduced flexibility at the network level, i.e., high liver fat markedly hampers the ability of the liver to adaptively regulate metabolism to meet excessive demands on basic liver functions.
Taken together, our findings suggest that the risk metabolic phenotypes are not always directly associated with the progression to the disease, but may also indicate an activation of the adaptive mechanism. Furthermore, our studies show that acquisition of a specific risk phenotype may lead to global changes in metabolic network properties such as reduced flexibility.

C1: Does the Placental Function Contribute to Fetal and Childhood Adiposity? Thursday 13th March, 11.50-13.25

Lipid-immune crosstalks at the maternal-fetal interface: Impact of obesity

EARLYNUTRITIONMEMBER

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Excess energy associated with obesity translates into molecular signals and low grade inflammation through the activation of innate immune networks. Pre-gravid maternal obesity and increased insulin resistance appear to be the strongest risk factors for increased fetal adiposity and metabolic dysfunction in childhood. Positioned at the maternal-fetal interface, the placenta is the primary target of all maternal derived signals. Based on these observations our team has developed the concept that obesogenic signals from pregnant women are triggers of altered feto-placental growth. The placenta of obese women gets infiltrated with macrophages. These macrophages then secrete a wide array of cytokines and other activators of innate immunity which contribute to impair placental function. Activation of innate immunity by endotoxin-lipopolysaccharides (LPS) has been proposed as a mechanism for enhancing immune pathways in the placenta.
Pattern recognition receptors of the toll-like receptor (TLR) family play a predominant role in activating innate immune pathways leading to metabolic inflammation. TLR4, the receptor for lipopolysaccharide (LPS) originating in gram negative bacterial walls, mediates the first innate response to exogenous pathogens by releasing inflammatory cytokines. The structure of the Lipid A hydrophobic side chain of LPS, which contains 5-7 fatty acid chains, suggests a role of TLR4 in also stimulating lipid sensing. A role of fatty acids to enhance metabolic inflammation and insulin resistance has been established in rodents. In this presentation, we will review state of the art evidence that in pregnancy with obesity, endotoxemia, inflammatory cytokines and excess maternal lipid substrates initiate concurrent immune pathways at the maternal-fetal interface.

A periconceptional maternal hyperglycemia disrupts the feto-placental membrane fatty acid profiles in a rabbit model

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Type-1 diabetes (T1D) is caused by the reduction in pancreatic insulin secretion, inducing chronic hyperglycemia. Pre-gestational T1D increases the risk of miscarriage and congenital malformations and programs the offspring to develop metabolic syndrome at adulthood. Management of maternal diabetes is essential during the gestation but could be highly important around the conception. The aim of this study was to explore the effects of maternal TD1 during the periconceptional period on feto-placental phenotype at 28dpc (term=31days), according to the sex of the conceptus.
Diabetes was induced by Alloxan in dams 7 days before mating. Glycemia was maintained at 15-20mmol/L with exogenous insulin injections. At 4dpc, embryos were collected and transferred into non-diabetic recipients. At 28 dpc, control (C) and diabetic (D) fetuses

were collected for biometric records and lipid analysis of feto-placental tissues by gas chromatography. Data were analyzed by principal component analyses. D-fetuses were growth retarded, hyperglycemic and dyslipidemic compared to C. A specific fatty acid signature was observed in fetal plasma. The composition of placental and fetal liver membranes differed according to maternal status and fetal sex. Tissues from D-fetuses contained significantly more omega-6 polyunsaturated fatty acids compared to C. No biochemical signature was observed in the immature fetal heart, but docosahexaenoic acid was decreased and linoleic acid increased in the cardiac membranes of D-fetuses, indicating a higher risk of ischemia. This study demonstrates that an exposure to high plasma glucose during the short peri-conceptional period reduces fetal growth and alters the lipid profiles in all fetal tissues.

Placental fatty acid transfer – a key factor of fetal growth

EARLYNUTRITIONMEMBER

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The functionality of the placenta may affect neonatal adiposity and fetal levels of key nutrients as long chain polyunsaturated fatty acids. Fetal macrosomia and its complications may occur even in adequately controlled gestational diabetic mothers (GDM) suggesting that maternal glycaemia is not the only determinant of fetal glycaemic status and wellbeing. We studied in vivo placental transfer of fatty acids (FA) labelled with stable isotopes, administrated to 11 control and 9 GDM pregnant women (6 treated with insulin). Subjects received orally ^{13}C-palmitic, ^{13}C-oleic and ^{13}C-linoleic acids and ^{13}C-docosahexaenoic acid (^{13}C-DHA) 12h before elective caesarean section. FA were quantified by gas chromatography (GC) and ^{13}C-enrichments by GC-isotope ratio mass spectrometry. ^{13}C-FA concentration was higher in total lipids of maternal plasma in GDM vs. controls, except for ^{13}C-DHA. Moreover, ^{13}C-DHA showed lower placenta/maternal plasma ratio in GDM vs. controls and significantly lower cord/maternal plasma ratio. For the other studied FA ratios were not different between GDM and controls. Disturbed ^{13}C-DHA placental uptake occur in both GDM treated with diet or insulin, while the last ones also have lower ^{13}C-DHA in venous cord. The tracer study pointed towards impaired placental DHA uptake as critical step, while the transfer of the rest of ^{13}C-FA was less affected. GDM under insulin treatment could have also higher fetal fat storage contributing to reduce ^{13}C-DHA in venous cord. DHA transfer to the fetus was reduced in GDM pregnancies compared to controls which might affect the programming of neurodevelopment in their neonates.

Exercise before and during an obese mouse pregnancy restores some placental gene expression and transport function

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Background: Overweight or obesity prevalence in pregnant women has increased in line with the global obesity epidemic: up to 50% of women of reproductive age and 20-25% of pregnant women at first antenatal visits in Europe and the USA. Epidemiological and animal data suggest that maternal obesity during pregnancy adversely affects offspring health. The underlying mechanisms may involve maternal and fetal dysregulation of glucose, insulin, lipid and amino acid metabolism. The placenta develops to support fetal growth, and therefore plays a key role in the aetiology of developmental programming by impacting on nutrient transfer.
Objective: The objective of this study was to analyse the effect of exercise on placenta in obesogenic diet exposed mouse dams.
Methods: The study consisted of 3 groups: control (n=5), obese (n=5) and obese + exercise (n=5). The obesogenic diet was for 6 weeks before first mating in the 2 obese groups. After weaning, the obese + exercise group, commenced training for a week (20 min/day, 5 days/week) before mating for second pregnancy and exercised until day 17 of gestation. The two other groups were also mated for second pregnancies. Placentas were collected at day 19 for morphometry/lipid staining and frozen for protein and gene expression analyses.
Results: Exercise intervention reduced placenta lipid storage and transfer to the fetal trophoblast. It also normalised expression of some insulin signalling components that were dysregulated in the placentas of unexercised obese dams.
Conclusion: Exercise starting before and maintained during pregnancy may improve fetal outcome by restoring placental nutrient transfer.

Placental transport and metabolism of amino acids

EARLYNUTRITIONMEMBER

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Amino acid transfer is complex process involving both membrane transport and metabolism. While these processes are understood in principle the effect of changing individual components in the system on the function of the system as a whole cannot be predicted. Computational modelling provides an approach which can represent the complex interactions underlying amino acid transfer. Amino acid uptake by the apical microvillous membrane of the placental syncytiotrophoblast requires interaction between accumulative transporters and amino acid exchangers. On the basal membrane amino acid exchangers and facilitated transporters are required to mediate efflux of amino acids. Transporter activity is dependent on amino acid gradients across membranes. These gradients are determined by: individual transporters, interactions between different transporters, maternal and fetal blood flow, mixing of blood within the different compartments and placental metabolism. These factors create a complex interplay between the different transport systems and between transporters and their local environment. This complexity means that while the principles of the system are known, how the system actually functions in practice cannot be intuitively understood. Mathematical modelling provides a mechanism by which these interactions can be represented and studied. Establishment of a model will allow exploration of the factors which result in impaired amino acid transfer and development of strategies to optimise placental transfer.

A2: The Influence of Stress and Stress-Nutrition Interactions during Pregnancy on Offspring Adiposity

Thursday 13th March, 16.15-17.50

Influence of diet and lifestyle during pregnancy on offspring bone mass and body composition

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Common chronic non-communicable conditions such as osteoporosis and obesity place a huge burden on society, with the cost of fragility fractures estimated to approach €40billion across Europe annually. Evidence is increasing that the environment experienced in utero may influence the intra-uterine and postnatal development of bone and body composition. Thus poor early growth predicts reduced adult bone mass and increased risk of hip fracture. Mother-offspring studies have suggested that factors such as maternal smoking, fat stores, physical activity and vitamin D status are determinants of bone mineral accrual and may influence postnatal fat and lean mass. Vitamin D appears a particularly important factor during pregnancy with several studies demonstrating reduced bone mass in children and adults who had been born to mothers with low circulating serum concentrations of 25(OH)-vitamin D in pregnancy. Epigenetic studies have provided further support for a role for vitamin D in early programming of skeletal development, and a large multi-centre randomised controlled trial is currently completing in UK, including over 1000 pregnant women randomised in a double blind design to either 1000 IU cholecalciferol daily or placebo, with offspring bone mass as the primary outcome. Such studies will help inform the value of strategies such as vitamin D supplementation in pregnancy for the optimisation of bone mass and body composition, with potential reductions in conditions such as osteoporotic fracture in future generations.

The maternal ingestion of sugar, fat and sodium during pregnancy is associated with the adiposity of children up to 18 months

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The evidence shows that maternal nutrition is related to adiposity in children and the potential risk of developing obesity and non-communicable chronic diseases in adulthood. We aimed to identify the association of dietary intake of sugar, fat and sodium during the third trimester of pregnancy with the adiposity between 3 and 18 months of life of the offspring. The dietary assessment was performed with 7-day food diary at 34 weeks gestation; and was analyzed using the DIAL program. Anthropometric measurements like triceps skinfold thickness (TST) and subscapular (SST), were obtained according to the WHO standards, at 3, 6, 12 and 18 months of life in the offspring. Multiple linear regression models were used for data analysis. Eighty-six mothers and their children were evaluated. We found that a maternal intake during third trimester of pregnancy high in fat, was associated with less decrease of TST from 3 to 18 months (R=0.740, b=-0.033, p=0.001), and less decrease of SST only from 3 to 6 months (R=0.373, b=-0.011, p=0.011). Likewise, there are association between intake of sugar and TST smaller decrease (R=0.714, b=-0.028, p=0.000) from 3 to 18 months, and between sodium intake and lower TST decreased (R=0.693, b=-0.001, p=0.000). The maternal sugar and sodium intake does not show association with the evolution of SST from 3 to 18 months. The minor decrease in TST is associated with increase maternal intake of sugar, fat and sodium during the third trimester of pregnancy, regardless of maternal nutritional status before and during pregnancy.

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Fetal glucocorticoid over-exposure: the key to developmental programming?

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Epidemiological and experimental evidence suggests an adverse fetal environment permanently 'programmes' physiology leading to increased risks of cardiometabolic, neuroendocrine and psychiatric disorders in later life. We originally hypothesised that fetal glucocorticoid overexposure might explain this link.
In inbred rodents, prenatal stress, glucocorticoid over-exposure or inhibition/knockout of 11ß-hydroxysteroid dehydrogenase type 2 (11β-HSD2), the feto-placental 'barrier' to maternal glucocorticoids, reduces birth weight and causes hypertension, hyperglycaemia, hypothalamic-pituitary-adrenal (HPA) axis hyperactivity and anxiety-related behaviours in adult offspring. The phenotype persists into a second generation and transmits via male and female lines, suggesting epigenetic mediation. While first and second generation phenotypes are similar, the molecular mechanisms and epigenetic marks differ implying strong selection on phenotype but arguing against neo-Lamarckian ideas of 'epigenetic inheritance'.
In humans, placental 11β-HSD2 activity also correlates directly with birth weight. Maternal glucocorticoid therapy or liquorice ingestion (which inhibits 11β-HSD) alters offspring cognition, affective behaviour and HPA axis function. Maternal exposure to extreme stress has similar effects and impacts are noted in the second, unexposed, generation.
Overall, the data suggest that developmental exposure to excess glucocorticoids/stress programmes peripheral and CNS functions in adult life, predisposing to pathology, effects which may impact on a subsequent generation. Any core mechanistic role for epigenetic processes in such early environment-induced individual differences remains to be confirmed.

Do even psychological pathways exist between certain perinatal factors and childhood obesity?

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Introduction: IDEFICS was a five-year multicentre study targeting obesity comprehensively in the 2-10 years age group. The importance of gestational weight gain (GWG) and birth weight (BW) in metabolic programming is well documented. Our aim was to discover whether "psychological programming" can be identified by associations between these perinatal factors and those maternal attitudes which contribute to childhood obesity.

Methods: From the baseline survey we analysed the data of children who were not preterm and the biological mother completed the parental questionnaire (N: 9035, boys: 49.5%, age: 6.0±1.81 years, BMI z score: 0.37±1.17 [mean±SD]). GWG was categorized according to the 15th-85th percentile of the sample, BW according to the 15th-85th percentile of WHO growth standards. Health attitudes (health-related locus of control [LC], wellbeing score of the child [WB], false assessment of the child's weight lower than real [FA]) were assessed by questionnaire. Correlations were controlled for income and maternal educational level.

Results: Significant relationship between GWG and BW with the present BMI z-score could be verified (p=0.002 and p< 0.001, respectively). GWG and/or BW correlated inversely with favourable health attitudes (WB: p=0.004; FA: OR=1.19 [CI:1.07-1.33], p=0.002) which in turn may influence later obesity (WB OR=1.26 [CI:1.17-1.58], p< 0.001; FA OR=5.49 [CI:4.91-6.16], p< 0.001). Some measures of LC showed similar correlations (p=0.028-0.001).

Conclusion: GWG and BW as phenomena with major impact may contribute to later childhood obesity not only via metabolic but also via psychological pathway by influencing maternal attitudes. The psychological pathway may offer a new target for intervention.

B.2: The Role of Paternal Factors in Determining Offspring Outcome

Thursday 13th March 16.15-17.50

Parental body mass index and childhood cardiovascular risk factors

EARLYNUTRITIONMEMBER

Romy Gaillard, Eric AP Steegers, Liesbeth Duijts, Janine F Felix, Albert Hofman, Oscar H Franco, Vincent WV Jaddoe

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Maternal pre-pregnancy obesity is associated with impaired cardio-metabolic health in offspring. Whether these associations reflect direct intrauterine, causal mechanisms remains unclear. In a population-based prospective cohort study among 4,871 mothers, fathers and their children, we examined associations of maternal and paternal prepregnancy BMI with childhood body fat distribution and cardio-metabolic outcomes, and explored whether any association was explained by pregnancy, birth and childhood factors. We measured childhood BMI, total body and abdominal fat distribution, blood pressure and blood levels of lipids, insulin and c-peptide. We observed that higher maternal and paternal prepregnancy BMI were associated with higher childhood BMI, total body and abdominal fat mass measures, systolic blood pressure and insulin levels, and lower HDL-cholesterol levels (p-values<0.05). Stronger associations were present for maternal than paternal BMI, with statistical support for heterogeneity between these associations. Also, maternal gestational weight gain, especially in early-pregnancy, was associated with these childhood outcomes. The associations for childhood fat mass and cardio-metabolic outcomes attenuated after adjustment for childhood current BMI. As compared to children from normal-weight mothers, those from obese mothers had increased risks of childhood overweight (OR 3.84 (95% CI:3.01, 4.90)) and clustering of cardio-metabolic risk factors (OR 3.00 (95%CI:2.09, 4.34)). As compared to children from normal-weight fathers, children from obese fathers had an increased risk of childhood overweight (OR 2.52 (95%CI:2.04, 3.12)), but not of clustering of cardio-metabolic risk factors. In conclusion, higher maternal and paternal prepregnancy BMI were associated with an adverse cardio-metabolic profile in offspring, with stronger associations present for maternal BMI.

Transmission by paternal line inheritance of metabolic and cardio-renal dysfunction to F2 offspring born to a growth restricted father

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Being born small increases cardio-renal and metabolic disease risk which are not limited to the first generation (F1) but can be transmitted to the next generation (F2) with limited evidence of paternal line transmission. We characterised cardio-renal and metabolic phenotype of F2 offspring born to normally grown and growth restricted (F1) fathers. Late gestation rat uteroplacental insufficiency was induced (Restricted) or sham (Control) surgery in F0. F1 males were mated with normal females. F2 offspring body weight was not different at birth but Restricted males were heavier than Controls at 4-6months with no differences in organ or adipose weights. Males, but not females, from Restricted fathers had altered glucose control following an IPGTT (higher area under glucose curve; reduced first phase

insulin secretion). Whilst Restricted F2 males were normotensive, evidence of increased left ventricular wall thickness (+11%) and concentric remodelling (echocardiography) emerged at 16months in the absence of altered heart contractility and left ventricular hypertrophy. Creatinine clearance was reduced in Restricted males.
F2 offspring, born to F1growth restricted fathers are not programmed to be born of low birth weight but developed altered glucose control in the absence of obesity. Although they remained normotensive, aged 16 month males developed concentric remodelling. Our findings provide novel evidence of transmission of metabolic effects, and early signs of an adverse cardiovascular phenotype with aging in F2 males via the paternal line in an uteroplacental insufficiency model of growth restriction. Females were protected from these programmed disease risks.

Genetic determinants of infancy and early childhood growth

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The high and rising prevalence of childhood obesity, even in very young children, has prompted efforts to identify its determinants and develop preventative strategies starting in early life. Genetic determinants of obesity have been increasingly identified in recent years through large-scale genome-wide association studies (GWAS); while these have been primarily performed in adults, notably these common variants also show major associations with childhood overweight and weight gain from infancy onwards, which is in keeping with the effects of rare genetic mutations on monogenic obesity. Findings from GWAS for puberty timing demonstrate the overlap in genetic susceptibility to overweight and early puberty, and also identify mechanisms linking rapid growth and development to later disease. Characterisation of early postnatal phenotypes, including growth, body composition and feeding behaviours, which are associated with these genetic variants may inform prediction and intervention strategies.

Paternal consumption of a selenium-deficient diet programs the susceptibility of female offspring to mammary carcinogenesis

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Recent studies show that paternal diet may program the susceptibility to non-communicable diseases in the offspring and selenium has been highlighted as an important micronutrient for mammary cancer prevention. We aimed to evaluate whether paternal diet, deficient or supplemented with selenium, could influence the susceptibility of female offspring to mammary carcinogenesis. Male Sprague-Dawley rats were fed AIN93-G diet containing 0.05ppm (deficient diet), 1ppm (supplemented diet) or 0.15ppm (control diet) of sodium selenate, for 9 weeks, during sexual development and maturation periods. They were mated with female rats consuming a commercial diet. At 7 weeks of age, their female offspring received 7,12 dimethylbenz[a]antracene for mammary tumor induction. At 13 weeks of age, the fathers fed a selenium-deficient diet showed lower ($p < 0.01$) plasma and red blood cells selenium concentration and higher ($p < 0.01$) glutathione peroxidase activity compared to control and supplemented diet fathers. Fathers fed a selenium-supplemented diet presented higher ($p < 0.01$) red blood cells selenium concentration compared to control and deficient diet fathers. The female offspring from fathers that consumed a selenium-deficient diet showed higher incidence of mammary tumors compared to offspring of control and supplemented-diet fathers ($p \leq 0.05$). The offspring of selenium-supplemented diet fathers showed longer ($p \leq 0.05$) latency of 2nd tumor appearance compared to offspring of control and deficient diet fathers. These results show that paternal consumption of selenium-deficient diet increases the susceptibility to mammary carcinogenesis in female offspring, while consumption of a selenium-supplemented diet is suggested to have an opposite effect. The associated mechanisms will be further investigated.

Paternal obesity, interventions and mechanistic pathways to impaired metabolic health of offspring

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Obesity and adverse related conditions, notably type 2 diabetes and sub-fertility are increasingly prevalent. It is now clear that the origins of developmental programming in the offspring originate not only from the mother but also from the father. Reports from our laboratories and others have now demonstrated a transmission of nutritional cues from the father to subsequent generations. Paternal high fat diet induced obesity, in the absence of diabetes, impairs glucose tolerance, induces insulin resistance and results in offspring obesity with earlier onset in females. The diminished metabolic health of the offspring is co-morbid with impaired reproductive function. The latter is transmitted through both parental lines to the second generation, as is insulin resistance through the paternal line to females and via the maternal line, to both sexes. Diet and exercise interventions in the obese father have been shown to partly alleviate the perturbations to the offspring phenotype. The mechanisms by which paternal exposures impact on offspring long term health are unknown, however, sperm and epigenetic changes are clearly implicated as the mediators of transmission of such paternal exposures. We have determined that founder male obesity alters acetylation of the germ cells in the testes, reduces germ cell global methylation and alters the abundance of microRNAs in both testes as well as in mature sperm. Together this provides evidence that the nutritional status of the father directly affects the epigenome of sperm.

C.2: Epigenetics, Diet and Metabolic Programming

Thursday 13th March, 16.15-17.50

Maternal hyperglycaemia and foetal epigenetic adaptations

Marie-France Hivert

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There are increasing evidences that prenatal events influencing in utero milieu and foetal development are associated with risk of developing chronic adult conditions such as obesity, diabetes, and cardiovascular diseases. Epigenetics is one of the potential molecular mechanisms explaining this phenomenon, often called 'foetal metabolic programming'. Epigenetics is defined as heritable regulation of DNA transcription that is independent of the DNA sequence and include DNA methylation. A few human studies have investigated associations between epigenetic marks in the offspring and maternal nutritional status. Maternal diabetes can be view as a state of 'over' nutrition as excess glucose crosses the placenta and influence foetal growth and development. This session will present the recent and on-going studies investigating associations between maternal hyperglycaemic states and epigenetic adaptations in offspring in candidate genes and genome-wide approaches.

High-fat diet during pregnancy and lactation alters DNA-methylation of key genes in lipid metabolism resulting in loss of protection from obesity in Gipr -/- mice offspring

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Ablation of the glucose dependent insulinotropic polypeptide receptor in mice (Gipr-/-) is protective of high-fat diet (HFD) induced obesity. We showed that Gipr-/- exposed to HFD during pregnancy (IU) and lactation (L) are no longer protected from diet induced obesity in adulthood. We now hypothesized that these programming effects are due to altered promoter methylation leading to decreased expression of key genes of peripheral fat oxidation. Male Gipr-/- offspring exposed to HFD or control diet (C) during IU/L were kept on normal chow for 22 weeks after weaning, followed by HFD for 20 weeks, resulting into Gipr-/- exposed to either C (KO Ciu-HF) or HFD (KO HFiu-HF) during IU/L and HFD in adulthood. Wilde type (WT) mice fed C during IU/L and HFD in adulthood served as controls (WT Ciu-HF). At 45 weeks of age, gene expression of fatty acid oxidation in muscle was analyzed by qRT-PCR. DNA-methylation was determined using mass spectrometry.

Gene expression of PPARα (2.45-fold) and CPT-1β (1.53-fold) was massively increased in KO Ciu-HF compared to WT Ciu-HF mice ($P< 0.05$), but down regulated by 45.2% for PPARα and by 41.0% for CPT-1β in KO HFiu-HF compared to KO Ciu-HF ($P< 0.05$) in muscle. We identified one CpG-site for PPARα and three CpG-sites for CPT-1β which showed a decrease in methylation in KO Ciu-HF compared to WT Ciu-HF and a renewed increase in KO HFiu-HF as seen in WT Ciu-HF. CpG-methylation was inversely correlated with gene expression. We conclude that fetal programming targets GIP-regulated metabolic pathways.

Intergenerational epigenetic inheritance in a murine model of undernutrition

Elizabeth J. Radford [1], *Mitsuteru Ito* [1], *Hui Shi* [1], *Jennifer A. Corish* [1], *Kazuki Yamazawa* [1], *Elvira Isganaitis* [2], *Stefanie Seisenberger* [3], *Timothy A. Hore* [3], *Wolf Reik* [3], *Serap Erkek* [4-6], *Antoine H. F. M. Peters* [4,5], *Thomas Down* [7], *Mary-Elizabeth Patti* [2], *Anne C. Ferguson-Smith* [1]

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The pre and postnatal environment can affect both an individual's risk of adult onset metabolic disease and that of subsequent generations. Although animal models and epidemiological data implicate epigenetic inheritance, little is known of the mechanisms involved. In a robust intergenerational model of developmental programming, we demonstrate that the nutritional environment experienced by F1 generation embryos in utero, solely during late gestation, alters the DNA methylome of the F1 adult male germline in a locus-specific manner, without affecting overall methylation levels. Differentially methylated regions are predominantly hypomethylated and enriched in nucleosome-retaining regions. A substantial fraction of these regions is resistant to early embryo methylation reprogramming, and thus has the potential to alter F2 generation development. Thus, in utero nutritional exposures during critical windows of germ cell development can permanently alter the male germline methylome, which may contribute to paternally-mediated development of metabolic disease in the subsequent generation.

Genome-wide differential DNA methylation profiling of obese and lean teenagers in Finland

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Introduction: Genetic loci associated with obesity related traits explain only a small fraction of the total variance in body mass, suggesting additional involvement of epigenetic factors. Epigenetic regulations of adipogenesis and co-variation between body mass index (BMI) and differential methylated sites have been demonstrated.
Aim: To identify differential methylation genome wide between obese and lean teenagers, utilizing samples from The Finnish Health in Teens (Fin-HIT) study.
Methods: Preliminary data from the pilot dataset (N=1711) show that 15% of Finnish 11-year-olds were overweight (BMI>21) and 8% were obese (BMI>23) in 2012. Bisulphite sequencing of saliva samples from 52 obese/overweight and 52 lean (BMI < 15, i.e. 10-percentile) of the 11 year-olds, identified methylation levels of all cytosines throughout an 84 megabase genomic target. Bismark bisulphite read mapper and MethylKit R package were used for analyses.
Results: We have generated 5 billion sequences, 170 billion methylation calls, and on average covered about 3 million CpG sites, more than 10 times per sample. 27 CpG sites and 461 1-kilobase genome tiles are differentially methylated (SLIM adjusted P value < 10-8). 19 of these sites are hypo-methylated and 8 are hypermethylated in obese teenagers compared with lean teenagers.
Conclusion and future perspectives: Identification of these differential DNA methylated sites and regions in lean and obese teenagers contribute to an increased understanding of non-genomic risk factors of obesity. Analyses of pathway enrichment and the genomic landscape surrounding these sites and regions, will be presented and may shed light on the biological pathways involved.

Analysis of genome wide DNA methylation patterns to identify mechanisms of nutritional programming

Eva Reischl [1,2], *Peter Rzehak* [3], *Sonja Zeilinger* [1,2], *Hans Demmelmair* [3], *Annette Peters* [1,2], *Melanie Waldenberger* [1,2], *Berthold Koletzko* [3]

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The early programming hypothesis proposes that environmental conditions during fetal and early post-natal development influence lifelong health through permanent effects on metabolism. Maternal nutrition might be one important factor for early life programming and some evidence exists from randomized nutritional interventions that nutritional intervention can have beneficial effects on health outcomes. Some first studies on methylation patterns as well as work in experimental animals suggest that epigenetic patterns are sensitive to the nutritional environment in early life and may thus be one mechanism underlying programming. Specifically, first evidence exists that long-chain polyunsaturated fatty acids (LC-PUFA) can induce epigenetic changes. We present a study, where we analyzed genome-wide DNA methylation patterns in human cord blood at delivery using the Illumina Infinium HumanMethylation450 BeadChip in relation to maternal dietary supplementation with fish oil during pregnancy. The aim of this project is to gain better insight into the molecular mechanisms taking place on the way from maternal nutrition during pregnancy to the offspring's later phenotypic outcome.

A.3: Increased Gestational Weight Gain vs. Pre-pregnancy Weight as Risk Factors for Childhood Adiposity

Friday 14th March, 10.45-12.20

Maternal and paternal body mass index and offspring obesity: A systematic review

EARLYNUTRITIONMEMBER

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Objectives and study: The intrauterine environment is proposed to have marked effects on body mass index (BMI) and adiposity in later life, which may be explained by the 'fetal overnutrition hypothesis'. We aimed to systematically evaluate the association of offspring BMI (or adiposity) at the age of >5 years with pre-pregnancy BMI (or adiposity) of the mother and BMI (or adiposity) of the father, and their relative contribution to predicting offspring BMI (or adiposity).
Methods: The MEDLINE, EMBASE, and Cochrane Library databases were searched in March 2012 for studies that evaluated the parent-offspring associations described above.
Results: Seven cohort studies were eligible for the final analysis. Among these, we identified 2 groups of trials that presented different data collected from the same cohorts of parents-offspring (The Avon Longitudinal Study of Parents and Children, ALSPAC and Mater-University Study of Pregnancy, MUSP). In total, 3 large birth cohorts and 1 additional small study were identified.
Only three studies provided a direct comparison of parent-offspring associations, with a statistically stronger maternal influence found only in the MUSP cohort.
Equivocal results were obtained from all studies describing the ALSPAC cohort. The parental effect (indirectly estimated by the reviewers based on the presented odds ratio) was similar in the Finnish cohort. In one additional small study, pregravid maternal BMI was found to be a strong predictor of childhood obesity.
Conclusion: Findings of our systematic review provide only limited evidence to support the 'fetal overnutrition hypothesis'.

Adherence to Mediterranean diet during pregnancy and childhood obesity at 4 years of age: Mother-child cohort study of Crete, Rhea study

Koinaki S. [1], Georgiou V. [1], Sarri K. [1], Karachaliou M. [1], Daraki V. [1,2], Vassilaki M. [1], Kogevinas M. [3,4,5], Chatzi L.[1]

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Background and aim: Considerable attention has been drawn to the developmental origins of childhood obesity. Maternal nutrition during pregnancy is an important indicator of fetal growth however, it remains uncertain whether this effect is apparent during childhood. The aim of this study was to examine the association of adherence to Mediterranean diet during pregnancy with childhood obesity at 4 years of age.

Methods: 527 mother-child pairs participating in the Mother-Child (Rhea) Cohort in Crete, Greece, were included in the present study. Maternal diet during pregnancy was assessed by a validated food frequency questionnaire and Mediterranean Diet (MD) adherence was evaluated through a priori defined score. Weight, height, waist circumference and skinfold thickness measurements (triceps, thigh, subscapular and suprailiac) were performed at 4 years of age. Multivariate log-poisson regression models were used to adjust for several confounders.

Results: One quarter of pregnant women had a high adherence to MD. Higher adherence to MD during pregnancy was associated with lower risk of increased fat mass (sum of 4 skinfold measurements ≥75th percentile; RR:0.59, 95%CI:0.38,0.91) and central adiposity (waist circumference ≥90th percentile; RR:0.67, 95% CI:0.46,0.99) at 4 years of age compared to women with low adherence to MD during pregnancy. Body Mass Index at 4 years of age was not found to be associated with maternal MD adherence.

Discussion: Maternal healthy dietary patterns during pregnancy may protect against excess adiposity and central obesity at preschool age.

Should overweight or obese women be encouraged to lose weight during pregnancy to improve fetal growth?

Andreas Beyerlein

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Restriction of gestational weight gain (GWG) has been discussed as a potential strategy to reduce adverse short- and long-term outcomes in pregnant women and their children. It has even been suggested that gestational weight loss (GWL) might be beneficial for overweight or obese mothers and their offspring. We assessed associations of GWL with pregnancy outcome stratified by maternal body mass index (BMI) category, including different obesity classes (class I, BMI = 30-34.9 kg/m²; class II, BMI = 35-39.9 kg/m²; class III, BMI ≥ 40 kg/m²). Using register data of 445,323 singleton deliveries in Bavarian obstetric units from 2000-2007, we calculated odds ratios (ORs) for adverse pregnancy outcomes by GWL compared with non-excessive GWG with adjustment for confounders. Outcomes were related to both maternal and offspring's health.

GWL was associated with a decreased risk of pregnancy complications, such as pre-eclampsia and non-elective caesarean section, in overweight and obese women. However, the risks of preterm delivery and small-for gestational-age births were significantly higher in overweight and obese class I/II mothers [e.g. OR = 1.68 (95% confidence interval: 1.37, 2.06) for small-for gestational-age births in obese class I women]. In obese class III women, no significantly increased risks of poor outcomes for infants were observed.

The association of GWL with a decreased risk of pregnancy complications appears to be outweighed by increased risks of prematurity and low birth weight in all but obese class III mothers, indicating that GWL is no safe strategy to improve fetal growth.

Excessive maternal weight gain during gestation leads to offspring with increased adipogenic potential in the immediate perinatal period in pigs

Donkin S, Ajuwon K.M.

Purdue University, Department of Animal Sciences, WEST LAFAYETTE, UNITED STATES

For many pregnancies in the United States, maternal weight gain is in excess of recommended range set by the Institute of Medicine. Limited data is available on the mechanisms linking excessive maternal gestational weight gain and increased obesity risk in the offspring. We have used a pig model to investigate the effect of excessive gestational weight gain and markers of adipocyte differentiation in the offspring. Gilts were fed either a normal (mNE) or a high energy diet (mHE) during pregnancy that led to a 30% increase in gestational weight gain. Piglets born to these gilts were weaned to either a normal (wNE) or high energy (wHE) diet. Subcutaneous adipose tissue samples were taken 48h after birth, at weaning (day 21) and at 3 months of age for determination of gene expression by RT-PCR. Expression of adipogenic genes such as PPARγ and CEBPα was not different between mNE and mHE offspring at 48h after birth, but was higher ($P < 0.05$) in mHE offspring at weaning compared to mNE. Additionally, soluble frizzle receptors (SFRP4 and SFRP5), were elevated in mHE offspring at weaning. At 3 months of age piglets fed wHE had higher ($P < 0.05$) backfat compared with wNE, but there was no effect of maternal diet on backfat and expression of adipogenic genes at this stage. In conclusion, excessive maternal weight gain during gestation results in higher adipogenic potential in the immediate perinatal period in the offspring, but these effects dissipate over time in the life of the offspring.

Paternal factors and newborn size and adiposity – impact of an antenatal to limit intervention gestational weight gain

EARLYNUTRITIONMEMBER

Julie A Owens, Lodewyk E DuPlessis, Andrea R Deussen, Rosalie M Grivell, Lisa N Yelland, Jodie M Dodd
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Maternal obesity and gestational weight gain (GWG) are well established as associated with macrosomia and increased infant and child adiposity. The influence of paternal weight and BMI on infant size and body composition has been far less studied, particularly in parental obesity. We therefore examined this in a triad subset of the standard care group of the LIMIT RCT, where 41% of women were overweight and 59% obese; and 23% of fathers were normal BMI, 42% overweight and 35% obese. After adjustment for maternal BMI and GWG, increasing paternal BMI did not affect size at birth, but was associated with increasing infant peripheral skin fold thicknesses and % body fat, particularly where paternal BMI > 35kg/m2. The extent to which this reflects shared genetics, a shared postnatal environment or developmental programming, as recently shown in animal models of paternal obesity, is not known. We also examined the effect of paternal BMI on the effect of the lifestyle (dietary and physical activity advice) intervention to limit GWG in overweight and obese women in the LIMIT RCT on infant outcomes. After adjustment for maternal BMI factors, increasing paternal BMI positively mediated the effect of intervention in reducing infant skin fold thicknesses and % body fat, particularly in infants of fathers in the highest BMI category. Understanding how the lifestyle intervention in mothers affects these paternal influences on infant adiposity, particularly in the most obese fathers, may reveal novel social or biological pathways for targeting during pregnancy, as well as in fathers pre-conception.

B.3: Unpacking Complexity in Etiology and Implementation of Interventions

Friday 14th March, 10.45-12.20

Systems Science to Guide Implementation of Whole-of-community Childhood Obesity Interventions

Matt Gillman

Type 2 diabetes after exposure during gestation to the Ukraine Famine of 1933

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The relation between pre-natal nutrition and adult health is much debated. For lack of direct measures, most studies use birth weight as an indicator of nutrition during gestation. If reported patterns reflect a causal relation has yet to be determined however because of the limitations of birth weight as an indicator of nutrition and the likelihood of confounding and bias in observational studies. To overcome these limitations, we used a 'quasi experimental' setting to compare the odds for Type 2 Diabetes (T2D) after famine exposure during gestation. Our study comprises 1,421,030 men and women born between 1930-1938 in nine regions of the Ukraine. Included are individuals born before, during, and after the Ukrainian famine of 1933 in regions with no, severe, and extreme famine exposure. Based on the 45,081 cases in this group listed in the national Ukrainian diabetes register in 2000-2008, individuals born in the first half year of 1934 in regions without famine exposure showed no increase in T2D odds (OR 1.00; 95% CI: 0.91-1.09) compared to births before or after the famine, individuals born in severe famine regions a 1.3 fold increase (OR 1.26; CI: 1.14-1.39), and individuals born in extreme famine regions a 1.5 fold increase (OR 1.47; CI: 1.38-1.58) . As the famine was the most extreme in the summer of 1933, this points towards the early gestation period as being particularly sensitive to nutrition disturbances with long term effects. Further studies will be needed to clarify the biological mechanism underlying these relations.

Emerging genomics technologies in research of complex diseases

André G. Uitterlinden [1,2,3],
Departments of [1] Internal Medicine, [2] Clinical Chemistry and [3] Epidemiology, Erasmus MC, ROTTERDAM, THE NETHERLANDS

The quantum leaps in scientific progress have frequently come from technological innovations, which can be referred to as the technology push. In the life-sciences this has been exemplified by the emergence of all kinds of "omics" technologies reflecting the capacity to analyse complete and complex molecular mixtures in a hypothesis-free approach, also known as "fishing expeditions" by more sceptical fellow scientists. Such approaches have been developed for DNA, RNA and protein molecules and the Human Genome Project has been the flagship project to highlight the successful use of such technologies. As a result many human disease areas have applied these technologies to progress biological understanding of disease mechanisms.
Driven by technological progress and concomitant shifts in research culture, gene discovery in complex diseases and traits has intensi-

fied in the past decade and led to some spectacular findings as a result of sequencing of human pedigrees with segregating Mendelian diseases and Genome-Wide Association Studies (GWAS). GWAS build upon (1) human genetic variation, (2) genotyping technology, (3) bio-banks, and (4) collaboration in consortia. I will discuss progress in this field, based on using cohort studies and consortia. Similar but more recent developments have taken place in the fields of RNA expression profiling and measures of DNA methylation, as examples of genomics technologies. The latest developments include the application of Next Generation Sequencing (NGS) technologies to analyse DNA sequence, RNA composition, and DNA methylation status in a variety of tissues. Such layers of genomic information can be used to annotate the human genome sequence to deepen our understanding. Finally, through NGS we are now unfolding the complex microbial ecosystems (of yeast and bacteria) in and on the human body, and investigating the influence of these intricate interactions on homeostasis and development of disease

Metabolic dysregulation in early pregnancy in association with offspring cardiometabolic risk in preschool children: The Mother Child "Rhea" Cohort in Crete, Greece

Daraki V. [1,2], *Georgiou V.* [1], *Chalkiadaki G.* [1], *Karachaliou M.* [1], *Koinaki S.* [1], *Sarri K.* [1], *Vassilaki M.* [1], *Papavasiliou S.* [2], *Kogevinas M.* [3,4,5], *Chatzi L.* [1]

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Background: Maternal pre-gestational body size is an important determinant of child growth, although few studies have examined the association of metabolic dysregulation in early pregnancy with offspring cardiometabolic risk.
Objective: To examine the association of pre-pregnancy maternal obesity and lipids' profile in early pregnancy with offspring obesity, blood pressure, and lipid levels at 4 years of age.
Methods: The present study includes 811 mother-child pairs participating in the Mother-Child (Rhea) cohort in Crete, Greece. Maternal BMI and fasting serum lipids were measured at the first prenatal visit (mean:12 weeks ± 0.7) Weight, height, blood pressure, abdominal circumference, skinfold thickness of triceps, thigh, subscapular and suprailiac, and non-fasting serum lipids were measured at 4 years of age. Multivariate Poisson-log and robust linear regression models were used to estimate the association of metabolic dysregulation in early pregnancy with cardiometabolic risk factors in preschool children, after adjusting for potential confounders.
Results: Pre-pregnancy overweight/obesity was associated with an increased risk for offspring overweight/obesity (RR:1.43, 95%CI:1.02,1.98), central adiposity(waist circumference ≥90th percentile: RR:1.74, 95%CI:1.09,2.79), increased fat mass (as measured by the sum of skinfolds: b-coef:5.28, 95% CI:2.45, 8.10), and high levels of systolic blood pressure (RR:1.30, 95%CI 0.91,1.87) at 4 years of age. An increase of 40mg/dl in cholesterol levels at first trimester was associated with increased risk of offspring overweight/obesity (RR:1.40, 95% CI:1.02,1.89) and dyslipidemia (cholesterol level ≥75th percentile: RR:1.29, 95%CI:1.00,1.67) at 4 years of age.
Conclusion: Maternal pre-gestational excess weight and hypercholesterolemia in early pregnancy may contribute to increased risk for the development of important cardiometabolic risk factors in preschool children.

Combining metabolomics and genetics data – a network approach

Jan Krumsiek
Helmholtz Zentrum München, MUNICH, GERMANY

This presentation will cover various techniques for the integration of metabolomics and genetics data, with a special focus on network-based analysis approaches. In the first step, relationships between metabolites are analyzed using Gaussian graphical models (GGMs), a data-driven correlation-based approach that we have previously demonstrated to recover true biochemical relationships from blood metabolomics data. In the second step, we perform genome-wide association studies (GWAS) with metabolites as quantitative traits. The GWAS results are combined with GGMs to generate an integrated network picture of metabolic and genetic interactions. This network visualization of the statistical associations provides a convenient and visually appealing way to analyze large-scale Omics data.
We will then discuss two applications of the integrated network approach. 1) The networks have been used to identify so-called 'unknown' metabolites, i.e. compounds which are reliably measured but whose chemical identity in the mass-spectrometry pipeline has not been validated yet. By investigating those unknown metabolites in the context of our integrated metabolic/genetic network, we can predict the most likely pathways those metabolites are involved in known, and in some cases even their specific chemical identity. For selected scenarios, we were then able to experimentally verify these predicted identities. 2) We further used the network approach in a large meta-analysis, combining around 8000 blood samples from two large European population studies. The integrated networks gave novel insights into the complex relationship between metabolism and genetics on a global scale.

C.3: Opportunities for Obesity Prevention in Early Childhood

Friday 14th March, 10.45-12.20

Priming of the obesity risk by smoking in pregnancy

Rüdiger von Kries
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Some 15 years there was some reluctance to believe that maternal smoking in pregnancy caused overweight in the offspring. State of the art epidemiological research, however, appeared to provide compelling evidence:
- Offspring of mothers, who started smoking after pregnancy, were not overweight.

- Adjustment for a number of confounders reduced the effect size: a clear and clinically relevant effect size persisted.
- Dose effects were reported.
- Replication of these findings in multiple settings allowing for meta-analyses providing effect estimated with narrow 95% confidence limits.
- Confirmation in animal studies.

This smelled almost as the proof of causality. Critical colleagues, however, frowned because paternal smoking was associated with similar size effect estimates. Even with adjustment for paternal smoking there was still a meaningful and significant association to maternal smoking in pregnancy, however. So was the association of paternal smoking adjusted for maternal smoking in pregnancy – despite much higher cotinine concentrations in the hair of newborns of mothers smoking in pregnancy. This does not match with the observation of dose effects. Studies on siblings with disjunctive exposure to maternal smoking during pregnancy provide a clue to adjust for "unmeasured" confounding. Two such studies have been published recently, showing that the effect of maternal smoking on childhood obesity either vanishes or becomes very small.
There are a number of reasons why mothers should not smoke in pregnancy. Unfortunately, however, avoidance of smoking in pregnancy is probably rather unlikely to provide a lever to battle the obesity epidemic.

Which costs does childhood obesity cause? Implications for obesity prevention in Germany

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Objective: The increasing prevalence of overweight and obesity in children has been linked to parallel increases in associated medical comorbidities, such as the metabolic syndrome, resulting in a major public health concern. This study quantifies lifetime excess costs of obesity in Germany as a representative European country acknowledging a history of obesity in childhood.
Methods: At stage 1 of the two-stage Markov model, the distribution of BMI categories was tracked from 3-17 years. At the starting point of stage 2, cohort members were distributed across two BMI categories (having been normal weight or overweight/obese). Starting at age 18, age-specific lifetime costs were simulated using two further Markov models. The German Interview and Examination Survey for Children and Adolescents (KiGGS) and the German Microcensus 2009 provided model parameter values. Cost estimates for overweight/obesity in childhood were identified by a systematic literature review.
Results: A history of obesity in childhood leads to substantially increased excess lifetime costs for men (26,071 EUR, 3% discounted 8,468 EUR; increase by 3) and women (25,622 EUR, 3% discounted 9,470 EUR; factor 4). Transition probabilities from overweight to obesity were especially high during childhood years and most obese children remained obese during adulthood.
Conclusions: Our results confirm that early childhood years might be crucial for reducing the economic burden of the obesity epidemic. Our models can serve as a starting point for evaluating cost-effectiveness of efforts to prevent overweight and obesity in early childhood.

Complementary feeding in infancy

EARLYNUTRITIONMEMBER

Veit Grote

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The complementary feeding period is a brief transition period embedded within a nutrition- sensitive period. During this period of rapid growth, dramatic nutritional changes take place. The infant transitions from a period of continuous nutrient supply from breast- and formula milk alone to explore a great variety of foods with differing nutritional content and quality. While the proportion of energy from fat strongly decreases, the intake from protein and, especially, carbohydrates increases. There is no indication that the timing of introduction of complementary feeding has a major impact on obesity risk. High protein and energy intakes during complementary feeding might be related to later adiposity; however, it seems not to be linked to any specific types of foods or food groups. The only exception might be dairy products that have been weakly linked to later obesity. Adherence to dietary guidelines is associated with increased lean body mass, but not BMI or fat mass. Several studies have shown that food preferences in later life are formed during the complementary feeding period and might be in turn related to later obesity risk. Early parental feeding practices, socioeconomic and other familial characteristics at least partially explain obesity risk.
Overall, publications on the effects of complementary feeding on later health are scarce. Since young infants are dependent on adults for nourishment, parental attitudes and beliefs about infant nutrition and actual feeding practices directly influence infant nutritional status. Early nutrition interventions to prevent obesity should take nutrition belief systems, parental feeding styles, socioeconomic and educational status into consideration. National nutritional guidelines should be implemented, propagated and followed.

Protein intake in early childhood is associated with obesity and cardiometabolic health at school age: The Generation R study

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Background and objectives: Studies in adults suggest beneficial effects of high dietary protein intake on obesity, blood pressure, and lipid profile. Whether protein intake is related to cardiometabolic health in children is unclear. Therefore, we examined the associations of total, animal and vegetable protein intake in early childhood with cardiometabolic health at school age in 2,920 children participating in a prospective population-based study.

Methods: Protein intake was assessed with a food frequency questionnaire at the age of 14 months and was adjusted for energy intake. Body mass index (BMI), body fat percentage (BF%, assessed with DXA), blood pressure, cholesterol and triglyceride levels, and insulin and C-peptide levels were measured at the age of 6 years.
Results: Intakes of total and animal, but not vegetable, protein were associated with higher BMI and BF% in girls (0.11 (95%CI 0.03, 0.19) SD increase in BF% per 10 g animal protein intake), but not in boys. Intakes of both animal and vegetable protein were associated with lower triglyceride levels in boys (-0.19 (95%CI -0.29, -0.08) SD in triglyceride levels per 10 g animal protein intake), but not in girls. Protein intake was not associated with childhood blood pressure, cholesterol, insulin or C-peptide levels.
Conclusions: Higher protein intake in early childhood is associated with a higher body fat percentage in girls and lower triglyceride levels in boys at the age of 6 years. Further studies are needed to investigate whether protein intake in early life affects the risk of cardiometabolic diseases in later life.

Nutritional challenges and opportunities during the weaning and toddler period

EARLYNUTRITIONMEMBER

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The early years of life are a period of very rapid growth and development. In addition, food preferences are formed which track into childhood and beyond. In this critical phase of life, the foundation is laid for a healthy life. An excess of energy, unbalances in macronutrient quality or nutritional deficiencies are inappropriate nutritional signals, which may lead to metabolic disturbances or the onset of obesity. The intake of protein and sugar sweetened beverages by young children for example, has been associated with an increased risk of overweight and obesity [1, 2]. In reality, dietary intakes of vegetables, alpha-linolenic acid, docosahexaenoic acid, iron, vitamin D and iodine are low [3, 4] and the intakes of protein, saturated fatty acids and added sugar are high in young children living in Europe [5-7]. A focus on improving feeding habits and balancing nutritional intakes early in life may have significant public health benefits.

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A.4: Mechanistic Insights from Animal Studies

Friday 14th March, 14.30-16.05

Programming by maternal diet-induced obesity – Mechanistic insights for intervention strategies

EARLYNUTRITIONMEMBER

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It is well established, through studies in humans and animal models, that events in very early life can influence the risk of an individual developing conditions such as type 2 diabetes, insulin resistance and cardiovascular disease. To date much focus has been directed towards the effects of maternal under-nutrition on the long-term health of the offspring. However in light of the growing epidemic of obesity, including in women of child-bearing age, attention has now been directed towards understanding the effects of maternal over-nutrition during pregnancy and lactation on the offspring. To address this we have used a mouse model of maternal diet-induced obesity where pregnant and lactating mice are fed a diet rich in saturated fats and simple sugars (reflective of a human westernized diet) to induce obesity. We have shown that this maternal dietary manipulation leads to cardiovascular dysfunction and insulin resistance in the offspring and have identified programmed changes in insulin signaling protein expression that may underlie these effects. As well as utilizing the mouse model as a tool to identify mechanisms through which programmed changes in the offspring arise, our recent studies have also utilized it to identify factors in the obese mother that mediate the detrimental effects in the offspring. Maternal hyperinsulinaemia, which is amenable to lifestyle interventions such as increased physical activity, has emerged as one important parameter. These findings in an animal model therefore provide important insight into rational intervention strategies that have the potential to prevent transmission of metabolic dysfunction between generations.

Perinatal nutritional programming of adipose tissue inflammation and metabolic dysfunction in diet-induced obesity

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Obesity causes adipose tissue (AT) inflammation and metabolic diseases in some but not all individuals. We tested whether perinatal overnutrition programs vulnerability to obesity-induced inflammation and metabolic dysfunction. Litters of C57BL/6 mice were reduced to 3 pups (SL) or maintained at 7 (NL) from postnatal day 4. NL and SL mice were fed normal chow (NC) or 60% high fat diet (HFD) from 5 to 17 weeks. Histology and flow cytometry were conducted on AT and data analyzed using 2x2 mixed effects ANOVA and reported as mean±S.E; p< 0.05* p< 0.01** p< 0.001***. SL-NC mice grew slightly larger than NL-NC (29.85±0.57g vs. 32.35±0.85*)

whereas SL-HFD became much heavier than NL-HFD (40.48±1.09g vs. 47.48±1.58***). HFD caused at least a 5-fold increase in epididymal, inguinal, and retroperitoneal depot weights (main effect***) with only inguinal being larger in the SL-HF compared to NL-HF*. Adipocyte sizes paralleled adiposity changes. Despite the modest differences in adiposity, all 3 fat depots in SL-HFD had more crown-like structures than NL-HFD (epididymal: 2.3±2.2 vs. 14.1±3.2***; inguinal: 0.3±0.7 vs. 2.2±1.0*; retroperitoneal: 9.6±3.7 vs. 23.7±5.2**). Epididymal fat from SL had greater total macrophage (195 x103±32 vs. 393±78 x103cells/g*) and M1 macrophage content (66x103±41 vs. 249x103±58cells/g**). The elevated inflammation in SL was associated with more pronounced hepatic steatosis (110±16 vs. 173±23mgTG/g*), fasting hyperglycemia (140±10 vs. 195±17mg/dl***), and glucose and insulin intolerances. These data suggest that overnutrition soon after birth may contribute to metabolic dysfunction in obese adults by directly programming the inflammatory response of AT rather than merely exacerbating obesity.

Mechanisms underlying programming by maternal obesity – The power of large animal models

EARLYNUTRITIONMEMBER

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Most of the studies conducted to evaluate developmental programming effects of maternal obesity (MO) on offspring have been conducted in altricial, polytocous rodents. There is a need for studies in precocial large animal models since many of the critical windows of developmental susceptibility to programming in rodents are post natal and occur in the presence of higher oxygen tension and glucose levels as well as a very different endocrine environment from fetal life when these same events occur in precocial mammals. We have developed a model of MO in sheep pregnancy, a precocial species commonly studied to evaluate developmental programming. Sixty days before conception, through pregnancy, parturition and lactation, control multiparous ewes were fed 100% of National Research Council (NRC) recommendations and MO ewes are fed 150% of the control diet. We have studied maternal, fetal and offspring effects and will present data on the fetal heart, neonatal lepton (in F1 and F2 offspring) as well as insulin and growth responses to post natal feeding challenges.
In this model maternal, fetal and offspring glucocorticoid activity is increased. And likely play a major role in the programming of obesity. We have also evaluated effects of an intervention in which MO ewes are returned to normal diet at the equivalent of 7 weeks or so of human pregnancy when interventions could be commenced. We demonstrated that reducing maternal diet of MO ewes to requirements from early gestation can prevent subsequent alterations in fetal growth, adiposity, and glucose/insulin dynamics.

Early supplementation of non-obese diabetic mice with oligosaccharides isolated from human milk reduces spontaneous autoimmune diabetes development later in life

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Human milk oligosaccharides (HMOS) have been implicated to affect immune function development. To investigate whether HMOS have the potential to affect the development of autoimmune conditions later in life, supplementation in early life was tested in mice that spontaneously develop autoimmune (type I) diabetes.
The total fraction of lactose reduced HMOS was isolated from pooled samples donated by healthy donors, and supplemented in AIN-93M diets at 10g/kg. Non-Obese Diabetic NOD/ShiLtJ mice were fed from week 4-10 on supplemented or control diet. Diabetes incidence was measured by urine glucose test. After two positive tests, or at 30 weeks of age, animals were sacrificed. Insulitis was analyzed histologically, lymphocyte populations were analyzed by flow cytometry. Supplementation with HMOS significantly reduced the incidence of diabetes up to the age of 30 weeks, as measured by urine glucose test (p=0.03). These findings were corroborated by pancreas histology and decreased T-cell activation marker expression in the spleen, although the ratio of Th1/Th2 cells remained unchanged. Surprisingly, spleen regulatory T-cells (CD4+CD25+FOXP3+) were reduced in the HMOS group as well. Temporary dietary exposure of NOD/ShiLtJ mice to HMOS in early life reduced the incidence of autoimmune diabetes later in life. The regulatory T-cell data suggest that the alterations are induced in response to the severity of the disease process, rather than being a causal factor of the protective HMOS effect. Overall, the results suggest that benefits of breast feeding may include changes in immune development by HMOS, leading to suppression of spontaneous autoimmune reactions later in life.

Role of feeding with slow digesting carbohydrates during pregnancy on improving metabolic health in the offspring: Mechanistic insights (NIGOHealth study)

EARLYNUTRITIONMEMBER

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Background and objectives: Maternal obesity prior to and through pregnancy program offspring to a broad spectrum of metabolic and physiological alterations later in life. This work summarizes preclinical results obtained up to date on NIGOHealth study. The main goal for this study is to evaluate the effects of feeding with slow digesting carbohydrates (SDC) during pregnancy on programming adiposity and muscle development in the offspring from obese mothers.

Methods: Rats were assigned to one of three experimental groups: Control dams fed a standard rodent diet before mating and throughout pregnancy; dams fed a high fat for 6 weeks before mating and then fed a HF diet containing either SDC or high digesting carbohydrates throughout pregnancy. Offspring's body composition and plasma biochemical markers were analysed by using MRI and bio-analyzer, respectively. Western blot was used to analyse signalling pathways. Muscle transcriptome, pathway and biofunction were analysed using the Agilent microarray and Ingenuity software.
Results: Offspring from pregnant rats fed with SDC showed changes on adipose tissue glucose transporters and insulin signalling, that were consistent with reduced adiposity at adolescence. Reduction on adiposity was associated to reduce levels of plasma glucose, triacylglycerides and cholesterol. Feeding with SDC during pregnancy also enhanced skeletal muscle development in the offspring.
Conclusions: Results from this study point out the importance of nutrition during critical periods of development and show the role of carbohydrate profile on maternal diet influencing key outcomes related to adipogenesis and muscle development in the offspring. This influence may translate into prevention of metabolic diseases and other alterations later in life.

B.4: Breast Feeding and Breast Milk Components - What is Important for Short and Long Term Development?

Friday 14th March, 14.30-16.05

A longitudinal cohort study to investigate associations between infant feeding and overweight into the adult years

EARLYNUTRITIONMEMBER

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Aims: The aims were to examine predictors of body mass index (BMI) in a prospective study of Australian children; to investigate relationships between inflammatory markers and components of a metabolic syndrome cluster; to examine adiposity in relation to breastfeeding using longitudinal analysis; to examine the infant feeding influence on adiposity rebound and tracking of BMI from birth; and to investigate potential early nutritional programming effects on growth trajectory patterns from birth to 6 years and later fat mass in adolescence.
Methods: Between 1989 and 1991 2,900 pregnancies were recruited at 16-18-weeks gestation into the Western Australian Pregnancy (Raine) Cohort study through King Edward Memorial Hospital in Perth, Western Australia. Children were comprehensively phenotyped from gestation to 23 years by a trained research team. Data collection included questionnaires completed by the primary carer and adolescent from 14 years, and physical assessments at all follow-ups. Duration of breastfeeding and exclusive breastfeeding were calculated based on the date that breastfeeding stopped and other milk was introduced.
Results: Breastfeeding for less than 4 months was significantly associated with adverse/rapid growth patterns.
Conclusion: Evidence exists for programming by nutrition in early infancy suggesting that there are windows of nutritional influence in relation to later health outcomes. Possible biological mechanisms for storing the 'memory' of early nutritional experience throughout life and its expression include adaptive changes in gene expression, preferential clonal selection of adapted cells in programmed tissues and programmed differential proliferation of tissue cell types.

Acknowledgment: The research leading to this presentation has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013), project EarlyNutrition under grant agreement n°289346, as well as from NHMRC- European Union collaborative project #1037966 Long-term influence of early nutrition on metabolic health 2012-2016.

Exclusive breastfeeding duration and cardiorespiratory fitness in children and adolescents

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Background: Breastfeeding (BF) has been associated with a protective effect against cardiovascular disease. Higher cardiorespiratory fitness during childhood is associated with healthier cardiovascular profile later in life.
Objectives: To examine the association of exclusive BF duration with fitness in youths and to test the role of body composition and socio-demographic factors in this relationship.
Study design: Exclusive BF duration was reported by mothers and categorized in 4 categories: bottle-fed, < 3 months, 3-6 months, and >6 months. Fitness was determined by a maximal cycle-ergometer test in 1025 children (9.5±0.4y) and 971 adolescents (15.5±0.5y) from Estonia and Sweden.
Results: Longer duration of BF was associated with higher fitness regardless of confounders (+5.1% L/min, country, sex, age, pubertal status and body mass index (BMI) adjusted $P < 0.001$ or fat mass and fat free mass (FFM) (+3.3%, adjusted $P < 0.001$). Further adjustment with birth weight, physical activity and mother educational level did not change the results ($P=0.001$). The results were consistent in youths with low ($P < 0.001$) or high FFM ($P=0.013$), in non-overweight ($P < 0.001$) or overweight ($P=0.002$), in offspring of non-overweight mother ($P < 0.001$) or overweight ($P=0.003$), with low ($P=0.004$) or high ($P < 0.001$) educational level and in participants born within upper ($P=0.001$), middle ($P=0.017$) or lower ($P=0.007$) tertiles of birth weight.
Conclusions: Longer exclusive breastfeeding has a beneficial effect on cardiorespiratory fitness in youths. As early infant feeding patterns are potentially modifiable, a better understanding of the possible programming effect of exclusive breastfeeding on cardiorespiratory fitness is of public health interest.

Lactation and intergenerational health of mothers and children

EARLYNUTRITIONMEMBER

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Breastfeeding duration and/or exclusivity could be a key to interrupting intergenerational mother-child vicious cycles of obesity. The question of whether having been breastfed causes less childhood or adolescent obesity is controversial. Potential mechanisms exist related to biological effects of breast milk or behavioral aspects of nursing. Many observational studies report that longer duration, exclusivity or preponderance of breastfeeding is associated with lower body mass or prevalence of obesity. However, recent evidence from studies with innovative designs, including 1 cluster randomized controlled trial to promote breastfeeding duration and exclusivity, suggest smaller or no effect compared with older studies. A related question is whether breastfeeding promotes return to pre-pregnancy weight in the mother and thus reduces risk of later chronic disease as well as obesity-related risks in any subsequent pregnancies. As with the children, however, this same cluster RCT found no effect of the intervention on maternal adiposity-related outcomes 11 years later. Overall the evidence for protective effects of breastfeeding on maternal and child obesity is weak. Nevertheless, promotion of breastfeeding appears beneficial for several important health outcomes, including atopy, gastrointestinal infection, and cognitive development.

Growth, nutrition and early programming of immune function in breast-fed infants and infants fed formula with added osteopontin (OPN)

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Breast milk contains a high concentration of OPN, which affects immune function. In contrast, infant formula is low in OPN. We performed an RCT in Shanghai, China to evaluate effects of adding bovine OPN to formula. Mothers chose to either breast (BF)- or formula-feed their infant from 1 to 6 months of age. Formula-fed infants received: control formula (FF), formula with 65 mg/L (F65) or 130 mg/L OPN (F130). Anthropometry was registered monthly and venous blood samples were taken at 1, 4 and 6 months of age. Hematology (RBCs, Hb, ferritin), immune parameters (FACS analysis, cytokines), plasma amino acids and BUN were analyzed. Antibody response to DPT vaccination was also used as a measure of immune function. Formulas were well tolerated and there were no significant differences in formula intake or growth among the formula-fed groups. Repeated measures analysis showed a higher % of T-lymphocytes and T-regulatory cells in infants fed F130 than infants fed the other formulas. FF infants had significantly higher levels of TNF-α than those fed F65 or F130 and BF infants. IL-6 levels were lower in infants fed F130 than in infants fed the other formulas and IL-10 levels highest in the FF group. These results suggest that addition of OPN to infant formula modifies development of immune function and cytokine responses of FF infants and makes them more similar to BF infants.

Breast milk and growth

EARLYNUTRITIONMEMBER

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Exclusive breastfeeding for the first six months of life is widely recommended because mother's milk provides the optimal nutrition for health, growth and development of the infant. Breast milk is a highly complex mixture of nutrients dissolved or emulsified in water. Composition varies between mothers depending on genetic and nutritional factors and it changes with the stage of lactation. While carbohydrate and protein content show only moderate intersubject variation, fat and many individual compounds show a high degree of variation. For many of these components it is unknown whether milk concentrations influence growth or long term health. Particular interest relates to milk fatty acid composition, as perinatal long-chain polyunsaturated fatty acid status may influence neurological development, immune system and obesity risk. The quantitatively minor lipid components glycerol-phospholipids and sphingomyelins as well as carnitine and its esters have the potential to influence nutrient absorption or metabolism, respectively. Human milk naturally contains peptide hormones, including insulin, insulin-like growth factors, leptin, adiponectin, and ghrelin which are important metabolic regulators. Although their concentrations are mostly low, some relationships of these hormones with infant anthropometry even after the period of breastfeeding have been established. It has been shown that overweight and obese mothers have increased levels of insulin in their milk which may affect the infant. Available breast milk samples from birth cohorts offer the opportunity to investigate the relationship between variation of major and minor breast milk components and variation of offspring growth and other disease risks.

C.4: The Role of Endocrine Regulation (Including Letin / Igfs) in Fetal and Postnatal Adiposity

Friday 14th March, 14.30-16.05

Maternal obesity and the developmental programming of offspring appetite and obesity: A role for leptin?

EARLYNUTRITIONMEMBER

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Mother-child cohort studies have established that both pre-pregnancy body mass index (BMI) and gestational weight gain (GWG) are independently associated with cardio-metabolic risk factors in young adult offspring, including increased adiposity. Animal models in

sheep and non-human primates provide further evidence for the influence of maternal obesity on offspring metabolic function, whilst recent studies in rodents suggest that perinatal exposure to maternal obesity may permanently change the central regulatory pathways involved in appetite regulation. Leptin signalling in the brain plays an important role in the hypothalamic control of appetite and energy expenditure via thermogenesis. But leptin also activates hypothalamic efferent sympathetic pathways innervating non-thermogenic tissues including kidney and liver and is implicated in the development of obesity-related hypertension and non-alcoholic fatty liver disease. Leptin also has a neurotrophic role in the development of the hypothalamus and neonatal hyperleptinaemia secondary to maternal obesity is associated with hyperphagia and permanently altered hypothalamic structure and function. In rodent studies maternal obesity alters neonatal adipocyte function and promotes an exaggerated and prolonged neonatal leptin surge associated with a persistent selective leptin resistance to the anorectic effects of leptin, combined with sympathoexcitatory hyper-responsiveness which is maintained into adulthood. Experimental neonatal hyperleptinaemia in naive rat pups provides proof of principle that hyperleptinaemia during a critical window in hypothalamic development may directly lead to leptin resistance, hyperphagia, adulthood obesity, and obesity-independently cardio-metabolic dysfunction. Insight from these animal models raises the possibility that early life exposure to hyperleptinaemia may be similarly detrimental secondary to obese pregnancy in humans.

Changes in neonatal nutrition modify hypothalamic leptin responsiveness in adult life

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Neonatal nutrition may modify circulating leptin levels, leading to changes in the maturation of hypothalamic circuitry, causing modifications of feeding behavior in adult life. Using the manipulation of litter size as a model of nutritional programing, we aimed to investigate in Wistar male rats the hypothalamic responsiveness to leptin. After birth, litters were adjusted as follows: small (3 pups-SL), normal (10 pups-NL) and large (16 pups-LL). On post-natal day 60, animals were treated with leptin (500µg/Kg ip) or saline at 5pm. Food intake and body weight gain were evaluated 12h after. In another set of animals, 40min after treatment, animals were perfused and the brains collected for p-STAT-3 labeling in the hypothalamus by immunohistochemistry (n=5-10). After leptin, NL rats reduced food intake (6.5±0.3 vs 7.8±0.3g/100g bw) and body weight gain (13.6±1.9 vs 21.2±1.1g). SL rats did not change food intake (7.4±0.3 vs 7.1±0.3g/100g bw) nor body weight gain (23.6±2.1 vs 24.1±3.4g) after leptin, compared to SL saline. LL rats showed a reduction in food intake (6.7±0.3 vs 8.5±0,8g/100g bw) and body weight gain (15.9±1.8 vs 22.9±1.8g), compared to LL saline. SL and LL rats had an increase in p-STAT-3 expression in the ARC in vehicle treated animals, compared to NL vehicle. Leptin increased p-STAT-3 expression in the ARC in NL rats and potentiated it in LL rats, but had no effect in SL rats. Our data suggest that changes in food availability during neonatal life modify hypothalamic leptin responsiveness in adulthood and may have long lasting effects on energy homeostasis.

Growth factors and their role in adipose tissue development in early life

EARLYNUTRITIONMEMBER

Michael E Symonds and Helen Budge
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There are three types of adipose tissue, brown, beige (or brown in white) and white, which have different molecular markers that can be depot specific. Brown adipose tissue (BAT) is the least abundant fat in the body but is characterised as possessing the unique uncoupling protein (UCP)1 which has the capacity to generate 300 times more heat than any other tissue. Adipose is one of the last tissues to appear in the fetus and BAT has the essential feature of enabling the newborn to effectively adapt to cool exposure of the extra-uterine environment. Its growth and development in the fetus is primarily regulated by a number of stimulatory factors which are each capable of ensuring the abundance of UCP1 peaks around the time of birth.
Significant depots of BAT are present both around central organs such as the kidney and heart but also in the neck or supraclavicular region. The extent to which these BAT depots are replaced by white adipose tissue or are transformed to a mix of beige and white adipocytes after birth remains a current focus of debate. Changes within adipose tissue, especially in early life can determine obesity onset. To date, the main processes in adipose tissue considered to be strongly influenced by epigenetics relate to the actions of microRNAs and long noncoding RNAs in the regulation of adipogenesis. Each fat depot has its own specific gene expression profiles as well as developmental growth trajectories which currently, do not appear to be driven by epigenetic changes.

Molecular mechanisms of renal dysfunction and hypertension secondary to neonatal hyperleptinaemia

☆ ***New Investigator Award***

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Division of Women's Health, Women's Health Academic Centre, King's College London and King's Health Partners, LONDON, UNITED KINGDOM

Maternal obesity in rodents leads to sympathetic mediated hypertension in the juvenile offspring and hyperphagia and increased adiposity in adulthood. This is associated with an exaggerated leptin surge in early postnatal life. We have investigated the origin of hypertension in neonatal hyperleptinaemic mice, including the mechanisms that lead to dysfunctions of the kidneys. Mice were injected with leptin (L-Tx, 3 mg/kg, ip) twice daily at postnatal day (PD) 9-14, to mimic the exaggerated leptin surge in neonatal offspring of obese dams, versus saline treated (S-Tx). Mean arterial pressure and glomerular filtration rate (GFR) were measured at 6 months of age using radiotelemetry and creatinine clearance test. After hypertension had been established, levels of tyrosine hydroxylase (TH), expression of AT1a and AT2R (ang II receptors), NHE3 (Na-H-exchanger 3), Nkcc2a (Na-K-Cl cotransporter), and COX-2 (cyclooxygenoase-2) were measured in renal tissue.
At 6 months of age, neonatal leptin wild-type mice demonstrated enhanced renal TH, renin and AT1aR expression, marked downregulated in AT2R, and decreased creatinine clearance [GFR ml/min gKW, L-Tx, 0.46±0.06 vs. S-Tx, 1.34±0.32, n=6, p< 0.01]. These alterations

were also associated with elevated proximal tubule Na-H exchanger 3 transporter. Interestingly neonatal leptin mice also demonstrated increased renal COX-2 expression [L-Tx, 458±92 vs. S-Tx, 162±37, n=6, p< 0.01]. COX has been associated with angiotensin II induced hypertension and reactive oxygen species (ROS).
Thus alterations in Ang II pathways and ROS handling in the kidney, may reset the tubular functions in neonatal leptin mice and underpin the development of hypertension and renal dysfunction.

Endocrine Programming of Hypothalamic Feeding Circuits

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The growing prevalence of obesity and associated diseases such as type II diabetes is a major health concern, including among children. Epidemiological and animals studies suggest that alteration of the metabolic and hormonal environment during critical periods of development is associated with increased risks for obesity, hypertension, and type 2 diabetes in later life. There is general recognition that the developing brain is more susceptible to environmental insults than the adult brain. In particular, there is growing appreciation that developmental programming of neuroendocrine systems by the perinatal environment represents a possible cause for these diseases. This talk will summarize the major stages of hypothalamic development and will discuss potential periods of vulnerability for the development of hypothalamic neurons involved in feeding regulation. It will also provide an overview of recent evidence concerning the action of perinatal hormones (including leptin and ghrelin) in programming the development and organization of hypothalamic circuits that regulate energy balance and adiposity.

A.5: The Role of Infant Feeding

Friday 14th March, 16.30-18.05

Qualitative developments in infant feeding – lessons from animal models

EARLYNUTRITIONMEMBER

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Mothers own milk remain the golden standard for feeding newborn infants, but how to formulate the best possible milk diet when mothers milk is not available? This seemingly simple question is still difficult to answer and much research is needed to clarify the role of specific milk components on short and long term infant health at many levels. Due to the difficulties in doing well-controlled studies in infants, studies in appropriate animal models may help. Results from models that are hypersensitive to small modifications in milk composition and its preparation will help to define the most important diet ingredients. We present a series of results from preterm pigs that have proven to be highly gut-sensitive in response to manipulation of diet ingredients (lactose, casein, whey proteins, essential fatty acids, minerals/vitamins, lactoferrin, pre-, pro- and anitibiotics) and diet treatments (e.g. spray-drying, pasteurizations). The results suggest that intact, raw milk products remain a better source of nutrients and gut health for hyper-sensitive newborns, than most formula product. Lactose, and its interaction with the developing gut microbiota, deserves more attention. Research should continue to better define the nutritive and gut protective factors in natural milk that are of benefit in newborn and growing infants.

Impact of nutrient density of formula on nutritional intakes in healthy term infants and the influence of home reconstitution

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Aim: of the present exploratory investigation was to evaluate the impact of nutrient density on nutrient intake based on data from a double-blind RCT studying the effect of three hydrolysed formulas on growth (analysis ongoing). Between 2-16 wks of age, infants were exclusively fed with powder formulas with different protein/energy ratio: 1.8, 2.0 and 2.27 g/100 kcal. At 4 and 12 wks formula intake was recorded during 7 days and bottles prepared by mothers were collected for nitrogen (EP Analyzer 428; Leco France) and fat ("Soxhhlet" Soxtec Aventi 2055; Foss) determination. Protein intakes calculated from nitrogen determination were compared to that estimated from the labelled values.
Results: 333 bottles were analyzed. Discordant results for fat and nitrogen contents (n=6) and formula intakes reported as < 100 or >220ml/kg body weight*day were considered as out of ranges (n=29) and were excluded from the final analysis (n=298). Protein intake (g/kg*d; mean±SD) calculated from the nitrogen content was significantly higher than that estimated from the labelled content at 4 (2.33±0.46 vs. 1.93±0.36, p< 0.0001) and 12 wks (2.24±0.39 vs. 1.83±0.33; p< 0.0001). Fat intake estimations were similar. Formula intake was inversely related to nutritional density (p< 0.0006) and weight gain (g/kg*d; n=132) was preferentially related to the mean energy intake estimated from chemical analysis (F=38.8) than to that from labelled values (F=24.3).Our study suggests that nutritional density, influenced by home reconstitution, significantly impacts nutrient intake. This needs to be considered in the interpretation of the results of nutritional studies performed in healthy term infants.

Effects of protein supply on child growth and body composition

EARLYNUTRITIONMEMBER

Martina Weber [1], Veit Grote [1], Annick Xhonneux [2], Jean-Paul Langhendries [2], Veronica Luque [3], Joaquin Escribano [3], Elvira Verduci [4], Enrica Riva [4], Dariusz Gruszfeld [5], Piotr Socha [5], and Berthold Koletzko [1] for The European Childhood Obesity Trial Study Group
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Protein as a key nutritional factor in the infant diets is an important regulator of infant growth. The multicenter European Childhood Obesity Project was designed to examine the effect of protein supply on anthropometric and metabolic development from infancy throughout childhood. Infants in five European countries were followed until six years of age. Formula fed infants were randomized to receive formula with the highest (HP) and lowest (LP) protein levels as regulated by the EU legislation of 2001 during their first year of life. Breastfed infants were followed as a reference.
Higher protein intakes were associated with rapid early growth, increased IGF-I levels in infancy, accelerated kidney growth and an increase of both body fat (fat mass index; FMI) and lean mass (fat free mass index; FFMI) at two years of age. At six years of age BMI, FMI, and FFMI were higher in the HP than in the LP group; the effect of a higher protein intake was more pronounced in FMI than in FFMI. This is seen in a significantly increased fat mass to fat free mass ratio. Body composition of the LP group resembled breastfed infants at six years of age.
Early nutritional programming of body composition and growth is modulated by protein supply in infancy. The opportunity to reduce body fat mass in early and late childhood by lowering the protein intake of infants offers a new preventive potential of childhood obesity.

Acknowledgement: Work reported herein is carried out with partial financial support from the Commission of the European Communities under the 7th Framework Programme, contract FP7-289346-EARLY NUTRITION. The reported results do not necessarily reflect the views of the Commission and in no way anticipate to the future policy in this area.

Iron and vitamin D deficiency in preterm babies - a potential programming link to cardiovascular disease in later life

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Preterm birth has been associated with increased risk of cardiovascular disease (CVD) in later life. It has been hypothesised that common micronutrient deficiencies in early life may contribute to CVD risk in preterm babies. Experimental data suggest that iron and vitamin D deficiency may alter development of the heart, vasculature and metabolic pathways resulting in altered function, thereby potentially leading to cardiovascular disease. The aim of this study was to determine the iron and vitamin D status of preterm babies after hospital discharge. Babies (< 37 weeks´ gestation) were recruited to the study 4 months after discharge. A capillary blood sample was analysed for haemoglobin (Hb), serum ferritin (SF), soluble transferrin receptor, C-reactive protein and serum 25-hydroxyvitamin D (25(OH)D) concentrations. Iron biomarkers and 25(OH)D were available for 61 and 49 babies respectively. Suboptimal iron status (Hb< 110 g/L and/or SF< 12 µg/L) was detected in 23.4% of the babies (n=14). Babies who received iron supplements had a significantly higher haemoglobin (123±8 vs 113±1 g/L, ***P***< 0.001) and serum ferritin (64.1±23.9 vs 40.2±24.4 µg/L, ***P***=0.001). All exclusively breastfed babies who did not receive vitamin D supplements (n=14) had a 25(OH)D ≤ 50 nmol/L whereas all babies who received infant formula had 25(OH)D ≥ 50 nmol/L. We conclude that suboptimal micronutrient status in preterm babies 4 months after hospital discharge is common. Optimising nutrition after discharge as well as in hospital may ameliorate the potential cardiovascular disease burden in survivors of preterm birth, a population that is increasing steadily worldwide.

Energetic efficiency of infant formulae

EARLYNUTRITIONMEMBER

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Differences between breastfed and formula-fed infants regarding growth velocities and nutritional intake have widely been described. Formula-fed infants show higher growth velocities, which has been associated with a higher risk of obesity and type 2 diabetes in later life. Results from several studies indicated, that rapid early growth seems due to a higher protein intake of formula-fed infants compared to breastfed infants. Besides differences in metabolism it has been found that the energetic efficiency (growth per 100 kcal) of breastfed infants is 11% higher than the energetic efficiency of formula fed infants. Less data is available on the importance of formula composition for the energetic efficiency of infant formulae. The importance of macronutrient composition or other factors of infant formulae for the utilization efficiency of dietary energy for growth has not been fully elucidated. Results from a randomized controlled trial in 213 healthy term infants until the age of 4 months indicated, that similar to growth velocities in early infancy, the energetic efficiency in formula-fed infants is mainly influenced by the dietary protein / amino acid composition. It is point towards efficiency increasing effects of replacing beta-lactoglobulin by alpha-lactalbumin and the higher content of tryptophan. In respect to growth velocities and energetic efficiency the protein component of infant formulae might be the most important factor of an infant formula. Thus, newly designed formulae with revised protein content and composition should be evaluated in randomized clinical studies including consideration of their energetic efficiency.

B.5 The Toxic Environment and Perinatal Programming of Obesity and Dysmetabolism

Friday 14th March, 16.30-18.05

Prenatal air pollution exposure, later growth and cardio-metabolic risk

Emily Oken

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Accumulating human epidemiologic evidence has linked traffic and industrial sources of air pollution to adverse birth outcomes including perinatal mortality, low birth weight, small for gestational age, and preterm birth. With an increasing percentage of the global population living in urban areas with high ambient air pollution, and with those living in rural areas turning to alternative solid fuel-burning energy sources in the context of increased energy prices, exposure to air pollution from both outdoor and indoor sources is ubiquitous. It is likely that air pollution has health effects similar to exposure to maternal tobacco smoke, which is similarly composed of mixtures of particles and gases. However, few epidemiologic analyses have examined implications of prenatal air pollution for outcomes beyond the neonatal period. In this talk I will review the global scope of air pollution exposures, components of air pollution, and methods of assessing air pollution exposure in the context of epidemiologic studies. I will discuss existing evidence regarding associations of pollution exposure with postnatal growth, obesity, and cardiometabolic risks, and likely mechanisms by which these exposures may act. I will provide specific examples and preliminary results from two longitudinal pre-birth cohort studies, one in a US city with moderate ambient pollution levels, and another in a Mexican city with substantially higher average exposures. Accumulating evidence for the obesogenic and endocrine disrupting properties of air pollution has implications for global health.

Associations of in-utero smoke exposure and breastfeeding behavior with later autonomic nervous system function at preschool-age - preliminary evidence for"autonomic programming"?

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Background: Recent studies indicate that changes in the autonomic nervous system (ANS) are associated with obesity in children. Early pre- and postnatal influences associated with obesity in children might therefore also affect children's ANS. We aimed to examine whether smoking during pregnancy and breastfeeding behavior were associated with preschoolers' ANS function.
Methods: Using cross-sectional baseline data of a large preschool study (n=774), children's parasympathetic function as measured objectively by 1-minute heart rate recovery (HRR) at preschool age was related to retrospectively assessed maternal smoking status during pregnancy and breastfeeding behavior. Linear regression (n=680, mean age 4.8 years, 50.8% boys) adjusted for age, sex, body fat, birth weight, health status, SES, immigrant background was undertaken.
Results: In comparison to children from non-smoking mothers who were breastfed for 6 months, HRR of children who were never breastfed was significantly reduced by -4.5 beats/min (-5.1%). HRR in children, whose mothers smoked before and/or after the awareness of pregnancy, was reduced by -4.9 bpm (-5.6%) and -3.9 bpm (-4.4%), respectively. Given a significant interaction between sex and pre-/postnatal variables, sex stratified analyses were undertaken. In girls (n=334), both breastfeeding and smoking during pregnancy had substantial and clinically relevant effects on HRR (never breastfed: -10.5 bpm (-12.8%; p=0.01; smoking during whole pregnancy: -8.7 bpm (-10.6%, p=0.03)). In contrast, in boys, none of the associations between pre- and postnatal factors and HRR were significant.
Conclusion: Different pre-and postnatal factors in early life might program children's ANS function. The vulnerability to such external factors might depend on sex.

Prenatal exposures to persistent organohalogen contaminants in relation to offspring adiposity and cardiometabolic risk factors at 20 years of age

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Background and aim: Animal studies have shown that developmental exposures to certain endocrine disruptors may interfere with pathways that regulate body weight. In humans, these findings have mostly been explored with respect to weight gain in early childhood. This study examined associations between maternal concentrations of organohalogen contaminants and offspring cardiometabolic-risk factors at 20 years.
Methods: A cohort of 665 Danish pregnant women recruited in 1988-1989 with offspring follow-up in 2008-2009. Blood samples were collected for 422 offspring attending clinical examination. Polychlorinated biphenyls (PCBs), dichlorodiphenyl-dichloroethylene (DDE) and hexachlorobenzene (HCB) and 12 perfluoroalkyl acids including perfluorooctanoic acid (PFOA) were quantified in serum from week 30 of gestation.
Results: PFOA was positively associated with anthropometry at 20 years in female but not male offspring. Female offspring of mothers in the highest (5.8 ng/mL) versus lowest quartile (2.3 ng/mL) of PFOA concentration had adjusted 1.6 kg/m2 (95%CI: 0.6, 2.6) higher body mass index at 20 years, corresponding to an approximately 3-fold increased relative risk of being overweight or obese. Positive associations ($p<0.05$) were also observed with PFOA and serum leptin, insulin and leptin/adiponectin-ratio in female offspring, while similar but

less precise associations were observed in males. Other perfluoroalkyl acids were not independently associated with offspring anthropometry. Indications of a modest positive association between PCBs and HCB with female offspring anthropometry were also observed but only after full adjustment for important host factors.
Conclusion: In utero exposure to some organohalogen contaminants may have long term adverse consequences on cardiometabolic health, particularly in females.

Organic food consumption and the risk of preeclampsia; results from the Norwegian Mother and Child Cohort Study

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Background: Little is known about potential health effects of eating organic food. The aim of this study was to examine associations between organic food consumption during pregnancy and the risk of preeclampsia among Norwegian women.
Methods: The present study includes 28,192 nulliparous women who were recruited to the Norwegian Mother and Child Cohort Study (MoBa) in the years 2002-2007 and had completed a general health questionnaire at gestational week 15 and a food frequency questionnaire at weeks 17-22. Information about preeclampsia was retrieved from the Medical Birth Registry of Norway. The exposure variables were self-reported frequency of organic food consumption in six main food groups. We estimated relative risk as odds ratios and controlled for confounding with multiple logistic regressions. Overall dietary quality was assessed as scores on a healthy food pattern derived by principal component analysis and included as a covariate.
Results: The prevalence of preeclampsia was 5.3% (n=1491). No associations with preeclampsia were found for high intake of organic fruit, cereals, eggs or dairy, or an index reflecting total organic consumption. However, women who reported to have eaten organic vegetables 'mostly' or 'often' had lower risk of preeclampsia than those who reported low organic use (crude OR: 0.76, 95% CI: 0.61, 0.96; adjusted OR: 0.79, 95% CI: 0.63, 0.99).
Conclusion: Consumption of organically grown vegetables during pregnancy was associated with reduced risk of preeclampsia. Future studies need to address possible causal relationships underlying the observed association.

Infants under double attack? The role of environmental toxicants and gut microbiota in rapid growth and childhood obesity

EARLYNUTRITIONMEMBER

Merete Eggesbø

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Early life is a susceptible period in which environmental influences may have lifelong effects, although so far most studies have focused on the role of nutrition in early life. However there is increasing evidence for adverse health effects of exposure to environmental toxicants in early life, amongst others on growth and obesity.
Animal experiments indicate that environmental toxicants with endocrine disruptive properties may be of special concern. One compelling study exposed stem cells to organotins and observed increased the number of adipocytes on behalf of the number of skeleton cells. Human studies are also emerging in which an association between pernatal exposure to toxicants and early infant growth and childhood BMI is seen. Prenatal DDE exposure showed a clear positive association with growth velocity at 2 years and with BMI at 6-8 years, with a much stronger effect in males than in females in a large multicentre study encompassing several thousand babies and their mothers. In contrast exposure to background levels of PCB reduced birth weight and growth velocity.
Recently it has been acknowledged that gut microbiota plays a role in early programming. Animal experiments have shown the critical importance of exposure to gut microbiota during early life for optimal development and later functions of diverse organsystems. In the Norwegian NoMIC cohort we found a significant association between the presence of specific microbes and microbial groups, in certain time windows, and the growth trajectory of the babies. A further goal in the NOMIC cohort is to study the complex interplay between diet, gut microbiota composition and toxicants.

C.5: Recommendations for Practice

Friday 14th March, 16.30-18.05

Guidelines, recommendations, etc. - Based on eminence or evidence?

EARLYNUTRITIONMEMBER

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'Eminence based medicine. The more senior the colleague, the less importance he or she placed on the need for anything as mundane as evidence. Experience, it seems, is worth any amount of evidence' (Isaacs D & Fitzgerald D. BMJ 1999).
A number of terms such as 'guidelines,' 'recommendations,' 'regulations,' 'standards,' as well as 'position papers' and 'opinions' exist. There is a distinction between these terms; however, they are commonly used interchangeably. Moreover, some of them have the power of law in some, albeit not all, countries. Regardless of the terminology, any of these documents might be 'eminence-based' or 'evidence-

based'. 'Eminence-based' means relying on the opinion of a medical expert or health official when it comes to health matters, rather than on a critical appraisal of relevant evidence. In contrast, 'evidence-based' means the use of current best evidence in making decisions about the care of individual patients. Too often clinical practice guidelines, or similar documents, are of poor quality or are eminence-based. Consequently, health care decisions might be based on biased or erroneous information. To ensure the quality of guidelines, standards for the development of evidence-based guidelines have been in development. They are now being adapted by an increasing number of organizations and scientific societies. Issues related to these standards which ensure objective, transparent, and scientific valid information will be discussed.

How can vulnerable people be reached to reduce adverse health-related perinatal programming effects?

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Background: People with low socio-economic status have an increased health-risk but are difficult to reach for preventive and health-promoting Public-Health interventions. Low-threshold access to this group, especially during pregnancy and early parenthood, is therefore imperative for effective early interventions. Using existing access via social assistance programs could be an option to ease delivery of health-related interventions.
Activities of the "Early Aid" in Germany offer free-of-charge intensive pre- and postnatal care via family midwives (FM) for families with an increased need for psycho-social support. While prevention of child neglect is the primary goal of that intervention, the aim of this study was to assess if this established approach can be used for interventions to prevent malprogramming.
Design: Quantitative data were collected by service-delivering FM regarding the use of health-services of the intervention participants; overall, 295 datasets from families residing in Hessen (Germany) were analyzed. Furthermore, three expert interviews with FM were conducted and analyzed using qualitative content-analysis according to Mayring.
Results: FM reported a great interest of participants in health-related topics. This was confirmed by the frequent request for maternal and infant nutritional counselling (81%) of the participants. However, use of breastfeeding counseling was lower (42%), and women with low educational status demanded breastfeeding counseling significantly less ($p < 0.05$).
Conclusions: Health and nutrition-related counselling appeared to be of great interest to this difficult-to-reach population group. Although not the primary focus of the described intervention, programming effects might be successfully addressed by using existing psycho-social support related access to these families.

The Southampton Women's Survey: From observational evidence to behaviour change interventions

EARLYNUTRITIONMEMBER

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The Southampton Women's Survey is a longitudinal birth cohort with data collected on the mothers before conception of the child. 12,583 women aged 20-34 years were assessed when not pregnant; 3,159 were then followed through pregnancy and the children are followed-up. Analyses have shown that women's dietary patterns change little through pregnancy and the quality of women's diets before conception is the strongest predictor of the quality of the diets of their infants and children. Variations in infant diet were subsequently related to childhood body composition and cognitive function. Focus group work showed the importance of partners/fathers in influencing women's and children's diets.
These findings placed a focus on improving diet and lifestyles before young people embark on pregnancy. We have developed a tool called 'healthy conversations' in which professionals can help enable people to improve their diets and lifestyles. This is currently being evaluated in Southampton. A further intervention, LifeLab, aims to engage teenagers in the importance of their diet and lifestyles on both their own health and that of their future children. Secondary school students visit LifeLab, a purpose built laboratory in an university hospital setting, both to learn about the long-term implications of their lifestyle choices and also to enthuse them with science as a subject. A cluster randomised trial is assessing the effectiveness of LifeLab. Both interventions aim to improve health and nutrition literacy at a crucial time in the lifecourse. They are already having an impact on practice at the local level.

Ludical activities, facebook interaction and instant messages for children with cardiovascular risk factors impacts both children and caregivers: A randomized clinical trial

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Fundação Universitária de Cardiologia RS Brazil, UFCSPA, Post Graduation Program in Cardiovascular Sciences, PORTO ALEGRE, BRAZIL

Objective: To access the effectivity of an education program for overweight and/or dyslipidemic children in improving LDL-cholesterol both in children and their caregivers.
Methods: Randomized clinical Trial with 93 children from 7 to 11 years. Intervention group (IG) received 10 weekly group encounters with children and parents or caregivers, including orientation and ludic activities about food, healthy family habits, physical activity and attitudes, a Facebook group and instant messages. In all activities resources were elaborated to address specific objectives and to use simple and low cost resources. Control group (CG) received usual individual outpatient management with a multidisciplinary team. Outcomes included blood pressure and lipid profile after intervention. Statistical analysis included ANOVA, repeated measures ANOVA and Mc Nemar test.
Results: Mean age was 9.13 ± 1.43 years, 52.7% were girls. LDL-cholesterol was abnormal in 17 (35.4%) of children in IG at baseline, re-

ducing to 5 (10.4%) after intervention, while in CG there was an increase of children with abnormal LDL($p < 0.002$). The LDL levels were abnormal in 8 (16.7%) of caregivers in IG and 7 (15.16%) of CG. After interventions, none of the caregivers of IG showed alterations, while in CG this number rose to 11 (24.4%).
Conclusion: An education program based in simple and low cost resources may be effective to reduce LDL cholesterol both in children and their caregivers, showing that intervention with children may have extended benefits to their families.

Nutrition research and food legislation – the role of EFSA

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In the EU the general principles of food safety and consumer protection are laid down in the framework of Regulation (EC)178/2002 of the European Parliament and the Council as a consequence of several crises in the food sector. This explains the weight that is put on risk assessment in this document and the importance of its being undertaken in an independent, objective and transparent manner. It is the legal basis for the establishment of a European Food Safety Authority (EFSA) which provides a comprehensive independent scientific view of the safety and other aspects of the whole food and feed supply chains, including animal health and welfare, and plant health, but should also provide scientific advice and scientific and technical support on human nutrition in relation to Community legislation and assistance to the Commission in Community health programmes. A scientific opinion from EFSA may be requested by the Commission, by the European Parliament and the Member States. These requests are initiated mostly by new scientific data, some of which may result from EU financed research projects, or by the availability of new foods/substances/technologies to be used in diets or the manufacture of food. At EFSA three scientific panels are mainly responsible for nutrition and diet related questions: The panels on Nutrition, Dietary Products and Allergies (NDA), on Food Additives and Nutrient Sources added to Food (ANS) and, to some degree, on Genetically Modified Organisms (GMO). Of these the NDA panel deals with interrelated tasks, the revision of dietary reference values for nutrients which has an impact on the revision of compositional criteria for foods for particular nutritional uses (FPNU), e. g. in the present directive for infant and follow-on formulae, and the scientific substantiation of proposed health claims for nutrients, ingredients, single foods or even diets. Opinions on the composition of FPNU need a broad scientific basis for criteria aimed at satisfying both nutrient requirements and dietetic purposes, and they may serve as the basis of either revising existing food legislation or setting up additional directives provided their integration into food law is accepted by Member States, the EU Commission, stakeholders and finally the European Parliament. The scientific substantiation of health claims focuses on the convincing evidence for a specific statement in relation to a food or ingredient and the answer is either "yes" or "no". EFSA has published during the last two years guidance papers for several categories of health claims with indications of relevant measures for different health outcomes.
EFSA is well aware that each one of its opinions may need revision in the future according to emerging new evidence.

A.6: Early Child Growth Trajectories as a Predictor of Childhood Obesity

Saturday 15th March, 10.10-11.45

Importance of characterizing growth trajectories

EARLYNUTRITIONMEMBER

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Characterizing the process of increasing physical size is critical to studying developmental origins of adiposity and long-term health. In contrast to measurements at one point in time, trajectories describe patterns of change in size as people age. One example of the need for trajectory analysis is the association of gestational diabetes with offspring obesity. Measuring body size only in preschool ages would miss the fact that offspring of diabetic mothers are heavier at birth and later in childhood, but not in between.
In studies of etiology or prediction, trajectories may serve as exposures (what is the association of this v. that trajectory on health outcomes?) or outcomes (what are the determinants of this v. that trajectory?). A long-standing practice in population research on growth is to use weight only, because it's widely available at many ages and is fairly accurate. But in fetuses and children, it's vital to disentangle weight from length/height, which is harder to measure. BMI (kg/m2) and other combinations of weight and length/height are useful in clinical and population research, but the curvilinear pattern of BMI change with age presents mathematical challenges. Alternatives include calculating age-specific BMI from separate weight and length/height trajectories. Recent advances in body composition measurement may allow analysis of their trajectories as well, which would provide more direct assessment of age-related changes in adiposity than weight and length/height can provide.

The effect of antenatal dietary and lifestyle advice on fetal growth in women who are overweight or obese: findings from the LIMIT randomised trial

EARLYNUTRITIONMEMBER

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Objectives: Overweight and obesity are recognized risk factors for fetal growth disturbances, with associated maternal and fetal risks. We aimed to assess the effect of an antenatal dietary and lifestyle intervention on fetal growth at 28 and 36 weeks gestation.
Methods: We conducted a randomised controlled trial evaluating the effect of a dietary and lifestyle intervention for pregnant women who were overweight or obese on maternal and infant health outcomes. Women were eligible for the LIMIT trial with a BMI ≥25kg/m², and a live singleton pregnancy. Fetal biometric growth measures (biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), femur length (FL) and estimated fetal weight (EFW)) were assessed prospectively at 28 and 36 weeks' gestation, and

Z-scores calculated for each fetus using the ASUM Ultrasonic Fetal Measurement Standards and the Hadlock C chart. Ultrasound measurements were analysed using linear mixed effects models, with adjustment for potential confounding factors. Statistical significance was assessed at the 2-sided p< 0.05 level. All analyses were performed using SAS v9.3 (Cary, NC, USA).
Results: Of women who consented to the LIMIT trial, 78 % attended for a research ultrasound at 28 (1733 scans) and 36 weeks (1713 scans) gestation. An antenatal dietary and lifestyle intervention did not result in any significant difference in biometric measures of fetal growth at 28 or 36 weeks gestation.
Conclusions: An antenatal dietary and lifestyle intervention does not result in any significant difference in fetal growth in the third trimester.

Metabolic markers, rapid growth and obesity at age 6 years

EARLYNUTRITIONMEMBER

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Early rapid growth is well established as a risk factor for later obesity. However, whether such growth is reflected in metabolic markers in infancy and whether such markers are associated with obesity in later childhood is much less clear.
For n=720 infants of the CHOP Study , a European multi-center randomized clinical trial and birth cohort of high-or low-protein content formula-fed and breastfed infants, 170 known lipid metabolites and amino acids were measured from serum samples drawn at age 6 months by FIA-MS/MS.
Each metabolite was regressed on the difference in weight, length and BMI measurements between 6 months and birth which were standardized according WHO-growth standards before subtraction. As a value of these standards indicate ideal growth at each age a positive value for the difference indicates a higher than "ideal" velocity in growth (rapid growth).
Growth related metabolites were identified by Bonferroni corrected P-values and those significant used as predictor(s) of BMI-SDS defined overweight (<90 percentile) or obesity (<97 percentile) at age 6 years by logistic regression.
Standardized weight-gain and BMI-gain was associated with several amino acids, acylcarnitines and phosphatidylcholines. However, much less of these metabolites showed also an association with obesity at age 6 years. Results regarding gain in standardized length and weight-for-length will also be explored and presented as well as analysis accounting for feeding group.
Most of these results support the DoHaD hypothesis of early metabolic programming however require further exploration, adjustment and in particular replication in further cohorts.

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Maternal 25-hydroxy-vitamin D status in late pregnancy and offspring muscle development: Findings from the Southampton Women´s Survey (SWS)

EARLYNUTRITIONMEMBER

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Background: Maternal 25-hydroxy-vitamin D [25(OH)D] status in pregnancy has been associated with offspring bone development and adiposity. There is evidence to support a role for vitamin D in muscle function, yet little is known about the role of antenatal 25(OH)D exposure in programming muscle development. We therefore investigated the associations between maternal serum 25(OH)D status in late pregnancy and offspring muscle mass and strength at 4 years of age.
Methods: The Southampton Women´s Survey is a prospective mother-offspring birth cohort study in Southampton, UK. Maternal serum 25(OH)D was determined at 34 weeks gestation. At 4 years of age, offspring body composition was assessed by Dual Energy Xray Absorptiometry (Hologic Discovery) and hand grip strength measured by hand dynamometry (Jamar Dynamometer). Physical activity was assessed by 7 day accelerometry (Actiheart). Associations were explored using linear regression to yield standardised beta coefficients (SD/SD).
Results: 678 mother-child pairs were included. Maternal serum 25(OH)D was positively associated with offspring height-adjusted grip strength (beta=0.10 SD/SD, p=0.013). This relationship persisted after adjustment for maternal factors, duration of breastfeeding and the child´s physical activity (n=326) (beta=0.13 SD/SD, p=0.011).
There was no significant association between maternal 25(OH)D and offspring total lean mass (beta=0.06 SD/SD, p=0.15), but a positive association with percent lean mass (beta=0.11 SD/SD, p=0.006). This was however attenuated by the addition of confounding factors (beta=0.07 SD/SD, p=0.062).
Conclusions: Antenatal exposure to 25(OH)D might influence muscle development through an effect primarily on muscle strength rather than muscle mass. Intervention studies are now needed to confirm this finding.

Cord blood biomarkers of the fetal metabolism: associations with postnatal growth and later metabolism

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Maternal metabolism during pregnancy impacts neonatal outcomes but also appears to be associated with specific child growth trajectories later in life. A better understanding of the growth trajectories subsequent to some fetal exposures and of the mechanisms at work is crucial. Gestational diabetes is one of the major risk factors for fetal macrosomia and has been associated with higher risk of overweight and obesity in the offspring in late childhood and adolescence. This could be explained by the tracking in body size from infancy into adulthood. Yet, evidence accumulates showing that children exposed to gestational diabetes have lower growth velocities in early life and that they are not significantly heavier in infancy compared to non-exposed children before 5 years. Besides, high insulin concentrations in the cord blood have been associated with slower growth in infancy, especially in girls. Other reports also suggest a negative association of cord leptin and adiponectin with infant growth. Thus, patterns showing relatively slow growth in infancy might be of interest in public health. Especially since slow growth in infancy has been associated with insulin resistance and diabetes in adulthood in the historical Finnish studies.

B.6 Physical Activity in Pregnancy

Saturday 15th March, 10.10-11.45

UPBEAT study: Association between physical activity in obese pregnant women and health of the offspring

Louise Hayes, Ruth Bell, Steve Robson, Lucilla Poston on behalf of the UPBEAT Consortium
Institute of Health and Society, Newcastle University, NEWCASTLE UPON TYNE, UNITED KINGDOM

Obesity in pregnancy is associated with offspring macrosomia, raised neontatal fat mass, and increased risk of obesity and diabetes in adulthood. Increasing physical activity during pregnancy could improve insulin sensitivity and reduce the risk of maternal and offspring adverse outcomes. The UK Pregnancy Better Eating and Activity Trial (UPBEAT) is a complex intervention (in 1546 obese pregnant women), designed to improve pregnancy outcome through dietary change and increased physical activity. Offspring are assessed at birth, 6 months and 3 years of age. No difference in physical activity was detected between women randomised to the intervention and control arm of the pilot trial (1). The relationship between sedentary behaviour and moderate and vigorous physical activity (MVPA) and infant body composition at birth was examined. Maternal sedentary time at recruitment was inversely associated with neonatal abdominal circumference. At 35-36 weeks' gestation maternal sedentary time was positively associated and MVPA inversely associated with neonatal abdominal circumference. Maternal physical activity is associated with infant body composition and is an appropriate target for intervention to improve infant outcomes. The challenge remains to develop an effective intervention to support obese pregnant women to be physically active.

Reference: (1) Poston, L., et al. (2013). "Developing a complex intervention in obese pregnant women; assessment of behavioural change and process evaluation through a randomised controlled exploratory trial." BMC Pregnancy & Childbirth **13**(1): 148.
UPBEAT is funded by (NIHR) (UK) RP-0407-10452.

Exercise before and during an obese mouse pregnancy restores maternal glucose tolerance

EARLYNUTRITIONMEMBER

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Background: Against a background of rising prevalence of overweight and obesity in women of reproductive age, epidemiological and animal data have shown that obesity during pregnancy programs adverse metabolic and cardiovascular outcomes in the offspring. We hypothesised: a) that maternal dysregulation of glucose, insulin and lipids drive this programming; b) that exercise intervention to the mother prior to and during pregnancy would improve maternal glucose homeostasis and therefore fetal outcomes.
Objective: The objective of this study was to analyse the effect of exercise on maternal glucose and lipid homeostasis in pregnant obese dams in late gestation.
Methods: The study consisted of 3 mouse groups: control (n = 5), obese (n= 5) and exercised obese (n = 5). Mice received an obesogenic diet for 6 weeks before first mating in the 2 obese groups. After weaning, the exercised obese group commenced training for a week (20 min/day, 5 days/week) before mating for second pregnancy and exercised until day 17 of gestation. The two other groups were also mated for second pregnancies. Body composition was analysed weekly during pregnancy. A glucose tolerance test was conducted at day 18. On day 19, dams were killed. Hysterectomised body and tissue weights and fetal/placental weights were analysed.
Results: Compared to their non-exercised counterparts, exercised obese dams demonstrated improved glucose tolerance, normalised serum insulin levels and reduced free fatty acid concentrations. Gonadal fat pad weights were also reduced.
Conclusion: Physical activity before and during pregnancy can improve glucose tolerance and insulin sensitivity in obese mice.

Physical activity before and during pregnancy and birth weight

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Normal fetal growth is a critical component of a healthy pregnancy and influence the long-term health of the offspring. Abnormal fetal growth and fetal growth restrictions in particular, have been linked to common lifestyle diseases such as type 2 diabetes mellitus and cardiovascular conditions in later life. Leisure time physical activity (LTPA) has the potential to reduce the risk of many complications of pregnancy and may be a modifiable factor contributing to birth weight. Current guidelines recommend healthy pregnant women to accumulate at least 150 minutes of moderate-intensity aerobic activity per week, independent of prepregnancy physical activity levels. Previous studies investigating the relationship between LTPA and birth weight were primarily concerned that LTPA during pregnancy would decrease birth weight or increase the risk of having a low birth baby (<2500 g). These concerns originate from early studies reporting a redistribution of blood flow to working muscles away from the uterus leading to reduced uterine blood flow. Reduced energy supply to the fetus during LTPA and exercise was also reported, because of increased maternal utilization of carbohydrates again leading to restriction in fetal growth. Even though birth weight is a broadly used perinatal outcome when studying the effect of LTPA during pregnancy, the results are inconsistent and few have examined the effect of LTPA on excessive birth weight. Hence, the aim of this talk is to summarize the literature on the effect of LTPA before and during pregnancy, across the birth weight distribution.

Maternal physical activity before and during pregnancy and offspring adiposity at mid-childhood

☆ ***New Investigator Award***

Kong K.L. [1], *Gillman M.W.* [2,3], *Rifas-Shiman S.L.* [2], *Wen X.* [1]

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Background: Maternal physical activity (PA) reduces birth macrosomia, but effects on offspring obesity are unknown.
Subjects/Methods: In Project Viva, women reported average leisure-time walking, light-to-moderate and vigorous PA before pregnancy and during the 2nd trimester. For total PA, we doubled vigorous activity and added it to the others. In mid-childhood (7-10 y), we measured height and weight, and DXA total and truncal fat mass index (FMI, TFMI). We assessed associations between maternal PA and offspring adiposity with multivariable models adjusted for maternal height, pre-pregnancy weight, medical/reproductive history, energy intake, and maternal/child socio-demographics.
Results: Among the 735 mother-child pairs, mean (SD) maternal PA before and during pregnancy were 11.8 (10.4) and 7.9 (8.2) h/week, and childhood BMI, FMI, and TFMI were 17.0 (2.8), 4.3 (1.8), and 1.4 (0.8) kg/m2. We did not find that higher maternal PA, before or during pregnancy, was associated with lower child BMI, FMI, or TFMI. For example, compared with 0-2 h/week PA in 2nd trimester, mothers with 3-10 h/week had children with FMI 0.23 kg/m2 higher (95% CI: -0.06, 0.53); for 11+ h/week FMI was 0.25 kg/m2 higher (-0.11, 0.61). In analyses of within-person PA change from before to mid-pregnancy, compared with decreasing 2+ h/week, maintenance of PA (± 1 h/week) was associated with 0.04 kg/m2 higher FMI (-0.27, 0.34); increasing 2+ h/week predicted 0.05 kg/m2 higher FMI (-0.29, 0.40).
Conclusions: Contrary to hypothesis, higher maternal PA before and during pregnancy, and change between them, was not associated with lower adiposity in mid-childhood.

Physical activity in early pregnancy and risk of gestational diabetes

EARLYNUTRITIONMEMBER

Marin Strøm

Centre for Fetal Programming, Dept. Epidemiology Research, Statens Serum Institut, COPENHAGEN, DENMARK

Aim: Our aim was to test the hypothesis of an inverse association of physical activity during pregnancy with development of gestational diabetes (GDM) in a large prospective cohort.
Methods: Complete data was available for 58662 pregnant women from the Danish National Birth Cohort. To ascertain the GDM diagnosis, hospital records were collected from all women suspected to have GDM in their index pregnancy based on registry diagnoses or self-reported diabetes in pregnancy. This led to the identification of 705 with a clinically confirmed GDM diagnosis. Physical activity in first trimester was assessed around gestation week 12 by a telephone interview. We present OR (95%CIs) from multivariable logistic regression models, adjusted for numerous potential confounders.
Results: There was an inverse association for physical activity with GDM for all measures of physical activity: adjusted ORs were 0.76(95%CI 0.62-0.94) for yes vs. no(ref); 0.62(0.39-0.97, p for trend 0.008) for ≥300 vs.0(ref) minutes total activity time; 0.66(0.46-0.97, p for trend 0.005) for highest quartile vs 0(ref) for MET-score. Adjustment for pre-pregnancy BMI attenuated the associations, and they became borderline significant. Stratification by pre-pregnancy BMI revealed that an inverse association for physical activity with GDM was present and statistically significant for women who were overweight/obese (BMI>25kg/m2) prior to pregnancy and not for women with pre-pregnancy BMI≤25kg/m2.
Conclusion: Physical activity in pregnancy might lower risk of GDM, primarily among overweight and obese women. On the other hand our results may reflect reverse causality: that high GDM risk women who become pregnant are more likely to be physically active.

C.6: The Contribution of Public Private Collaboration (PPC) to Translational Research

Saturday 15th March, 10.10-11.45

PPC (Public private collaboration): Benefits, challenges and risks from the perspective of Academia

*Mark Hanson**
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and NIHR Nutrition Biomedical Research Centre, University Hospital Southampton, SOUTHAMPTON, UK

NCDs represent a substantial financial and humanitarian challenge globally, both to Westernised societies and to low-middle income populations undergoing socio-economic transition. The potential costs to health are so large that there is an urgent case for deploying considerable resource to reduce risk in vulnerable groups. As recognised by the UN1, this requires concerted action by partnerships including governments, NGOs, civil society, academics and 'as and where appropriate' the private sector. The latter may be able to provide substantial resource, both in monetary terms and in-kind. The private sector also may be able to provide logistics and public communications expertise. This may be particularly helpful in initiatives to reduce later risk of NCDs in groups such as adolescents who are less amenable and accessible to existing public health channels.
Many questions arise. How and by whom can conflicts of interest in PPCs be identified, assessed and monitored? What is the most appropriate model for private sector engagement in NCD prevention – from philanthropy, through corporate social responsibility to collaboration? How can we clearly identify and coordinate the relative strengths of academic and private sector partners, and which organisation(s) should undertake such coordination? Are there pre-competitive opportunities for private sector companies to work together in certain areas to allow greater collaboration and, if so, how might they be operationalized?
I hope that this session will provide an opportunity to discuss these and related issues.

*This abstract represents the personal view of Mark Hanson.

1. United Nations General Assembly. Resolution adopted by the General Assembly. 66/2. Political declaration of the high-level meeting of the General Assembly on the Prevention and control of Non-communicable diseases. 2012

Driving science that matters through PPC: Examples of collaboration

EARLYNUTRITIONMEMBER

Ricardo Rueda
Strategic Research - Abbott Nutrition, GRANADA SPAIN

PPP in Nutrition Research constitutes a good model to make considerable and timely progress to improve public health. Forming strategic partnerships between private companies and leading institutions around the world, with the support of governments and funding agencies, enhances research productivity and effectiveness, accelerates innovation and drives new products to the market.
A key example of PPP for Abbott Nutrition (AN) is the Center for Nutrition, Learning and Memory (CNLM) at the University of Illinois Urbana-Champaign (UIUC), USA. The Center directs pioneering, multi-disciplinary research connecting cognition, brain function and nutrition, led by faculty at UIUC in partnership with leading global scientists and utilizing extensive supporting technologies.
Another example of partnership is Abbott facilities at university research parks located at UIUC and the University of Granada (UGR), Spain. In both locations, leads for key Abbott research projects are paired with postgraduate and undergraduate researchers to help Abbott extend research teams globally, explore new opportunities and accelerate research.
A third example of partnership is the research program Early Nutrition, which is funded by the European Union and is the largest project worldwide investigating programming effects for health in later life. AN participation involves multiple collaborations on six work-packages through the project entitled NIGOHealth (Nutrition Intervention during gestation and Offspring Health).
AN believes that partnerships through global networks will continue to generate innovative solutions for local and national public health nutrition issues. Together, we are moving forward, taking scientific advancements and quickly turning them into nutritional solutions and products that matter to consumers.

Public-private partnership insights from preclinical and epidemiological studies: tools to shape nutritional intervention trials

EARLYNUTRITIONMEMBER

Eline M. van der Beek
Nutricia Research, Danone Nutricia Early Life Nutrition, SINGAPORE

The rapid increase in non-communicable diseases (NCDs) like diabetes, obesity, allergy and cardiovascular disease cannot be simply explained by genetic or individual lifestyle factors only. Current scientific evidence links the development of an individual in early life to the risk of NCDs later in life. Exposure to specific environmental challenges during organ development may result in structural changes and changes in functionality of tissues altering the flexibility of the body to adequately respond to subsequent challenges.
Our scientific research efforts focus on understanding the role of nutrition and specific nutrients (or lack thereof) during pregnancy, infancy and toddlerhood. We aim to elucidate how these nutrition exposures with different timing and duration may impact different aspects of organ growth and development. Current collaborative epidemiological and preclinical research projects help us to understand how nutrition, i.e. specifically the quality of protein, fat and carbohydrates, affects early growth and body composition development as well as development of the brain, immune system and gut microbiota. The outcomes enable us to fine-tune clinical trial design by identifying appropriate target groups as well as distinct, measurable and clinically relevant end points and biomarkers to show beneficial effects of specific nutritional innovations. These nutritional innovations should be tailored to the environmental circumstances and specific changing needs of mother and child to ensure the right amount of the right ingredients at the right time.

WORKSHOPS AND SYMPOSIA

WS.1: Body Composition Assessment in Mother-Offspring Studies

Friday 14th March, 8.20-9.25

Using peripheral quantitative computed tomography to assess bone and body composition

EARLYNUTRITIONMEMBER

Rebecca Moon

MRC Lifecourse Epidemiology Unit, University of Southampton, SOUTHAMPTON, UK

Dual energy X-ray Absorptiometry (DXA) is a useful instrument to assess bone and body composition in epidemiological studies. In children, the low radiation exposure and minimal movement artefact make it ideal. However, DXA is limited by the conversion of a 3D structure into a 2D image, leading to overestimation of bone mineral density (BMD) in large subjects and underestimation in smaller subject. Conversely, peripheral quantitative computed tomography (pQCT) enables an assessment of true volumetric BMD and bone geometric properties. Furthermore, additional information can be obtained on soft tissue properties including subcutaneous fat thickness, muscle cross-sectional area and muscle fat density. Given the increasing recognition that fat depots have differing effects on cardiovascular and metabolic risk and musculoskeletal development, the complementary use of DXA and pQCT might further this understanding. In this workshop, I will aim to review the use of DXA and pQCT in children, delineating the potential caveats to each technique. By the end of the session, participants should have an understanding of the pros and cons of each method for assessing bone and body composition, and how they have been used in previous studies.

Air Displacement Plethysmography in infants and young children

EARLYNUTRITIONMEMBER

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Assessment of body composition during early life is an important clinical and research tool.
Air Displacement Plethysmography (ADP) has been shown to be a valid technique in infants, children and adults for the determination of body composition. ADP is a densitometric technique. With this technique, body mass and body volume are measured; mass is measured on an electronic scale, volume is measured in an enclosed chamber by applying gas laws (Boyle's law and Poisson's law) that relate pressure changes to volumes of air in the chamber.
The currently available ADP system for adults and children older than age 5 years is called the Bod Pod®. The system for infants younger than age 6 months (maximum weight: 8 kg) is called Pea Pod®. The Pediatric Option™ (a custom seat that can be fastened along the back of the chamber of the Bod Pod®) narrows the gap between the upper limit for the Pea Pod® and the lower limit for the Bod Pod®. The Pediatric Option™ can be used in children 2-6 years of age.
The methods to measure body composition currently available to researchers and clinicians have substantial drawbacks. The advantages of using ADP is that the measurements are noninvasive, fast, easy to perform, comfortable for infants and that it tolerates most infant behaviors, like crying or minor movement. It does not involve radiation exposure and does not require the infant to be immobilized or sedated. Practical aspects of the use of both the Pea Pod® and the Bod Pod® will be discussed during the presentation.

WS.2: Building an Electronic Data Capture System for a Clinical Trial (MedSciNet)

Friday 14th March, 8.20-9.35

Laima Juodvirsiene, Marius Kublickas, Magnus Westgren

MedSciNet UK, LONDON, UK

EARLYNUTRITIONMEMBER

MedSciNet is an international, Stockholm-based company with its roots in the Karolinska Institute, Sweden, and it specialises in the design, development and delivery of web-based IT solutions and services. Our customer base is within the medical and academic fields. Since 1995 when the company was founded, MedSciNet has delivered hundreds of solutions for clinical trials and medical registers worldwide. We will willingly share our expertise in how to plan and develop IT systems to collect clinical trial data. We will provide advice on what to consider in terms of data collection workflow, variable type selection, data checks, randomisation and patient identification. We will demonstrate what components are common for Electronic Data Capture (EDC) systems, what data monitoring and traceability capabilities can the system have, and how to prepare data for reporting and analysis. We will also provide examples of real-time systems. Recently MedSciNet has started providing applications to collect data via mobile devices - we will provide examples of them too, focusing on their capabilities. We will also demonstrate our current software tools to design and build eCRFs (electronic Case Report Forms) and to test, deploy and manage solutions that conform to FDA standards, guidelines and recommendations.

WS.3: Sensitive Windows for Gene Environment Interactions in Early Life – Do They Matter?

Friday 14th March 8.20-9.35

Early life drivers of the obesity epidemic?

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The obesity epidemic is usually considered a direct consequence of an obesogenic societal environment, promoting or facilitating a continuous positive energy balance by increasing availability of cheap, tasty, energy dense food and drinks and technical devices allowing reduction of physical activity, both at work and in leisure time. This environment is presumed to make people particularly exposed and genetically predisposed more obese. Obviously, no epidemic had developed if the environment did not allow for the energy supplies that is accumulated in the adipose tissue and even more so the supplies needed to meet the increased energy demands following the increased body mass. However, the question is whether this is what has driven the epidemic. In Denmark, we have been privileged to access data showing how the obesity epidemic among children and young adult men has developed since the interwar period. Denmark has had the same changes in obesogenic environment as most countries afflicted by the obesity epidemic, but the course of the development of the epidemic shows that these changes have not been the drivers of the epidemic. The data rather strongly suggest that changes in the early life - preconception, during pregnancy or infancy - has initiated and driven the epidemic. It is a major research challenge to identify and characterize these changes. As historically rather new changes embedded in our current society, it is likely that they are reversible, which provide promises to oppose the obesity epidemic in the future by prevention based specific early life interventions.

Nutrient-gene interaction in early life programming: Two examples

Eva Reischl [1,2], Marie Standl [3,4], Pauline Emmett [5], Berthold Koletzko [6], Joachim Heinrich [3], Colin Steer [5]

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[6] Department of Pediatrics, Dr von Hauner Children's Hospital, University of Munich Medical Center, MUNICH, GERMANY

Breastfeeding is considered as protective against allergy development and as beneficial for cognitive and neurodevelopment. Many ingredients are contained in human breast milk, but the responsible molecules that lead to the observed effects are not completely identified yet. Among the potential candidates are long-chain polyunsaturated fatty acids (LC-PUFA) that are contained in human breast milk and that possess important functions in inflammatory processes as well as neurodevelopment. Gene-nutrition interaction studies can provide links to causal relationships between nutritional influences and complex outcomes such as allergies and neurodevelopment. We analyzed the interaction between breastfeeding and genetic variants of the delta-5 and delta-6 fatty acid desaturases (encoded by FADS1 and FADS2), which endogenously process fatty acids contained in breast milk, on asthma prevalence and measures of neurodevelopment. Results from the ALSPAC cohort suggest that child FADS genotypes modulate the effect of breastfeeding on measures of intelligence achieved at school age. In addition, we observed interaction effects between breastfeeding and FADS genotypes on asthma prevalence until age 10 years in the GINI and LISA cohort. Our results corroborate the importance of breast milk LC-PUFA for neurodevelopment and protection from allergic diseases.

Impact of a diabetic intrauterine environment on childhood growth

Sandra Hummel and Anette-G. Ziegler

Institute of Diabetes Research, Helmholtz Zentrum München and Forschergruppe Diabetes, Klinikum rechts der Isar, Technische Universität München, MUNICH, GERMANY

Offspring of mothers with Gestational Diabetes Mellitus (GDM) have been shown to have a high risk for overweight during childhood. As the prevalence of pregnancies complicated by GDM is increasing, the number of children at high risk for overweight combined with a high risk to develop GDM themselves will also further increase. This intergenerational vicious cycle contributes to the epidemical development of obesity and type 2 diabetes.

The mechanisms beyond the reported association of maternal diabetes during pregnancy and increased risk for childhood overweight are still unclear. The fuel-mediated teratogenesis hypothesis proposes that intrauterine exposure to hyperglycemia causes permanent fetal changes resulting in excessive weight gain. However results from our German prospective cohort studies show that 1. prevalence of childhood overweight is significantly higher in offspring of GDM mothers compared with offspring of mothers with type 1 diabetes indicating that hyperglycemia per se does not increase overweight risk in the offspring and that 2. irrespective of birth size, which is an indicator of maternal glucose homeostasis during pregnancy, maternal pregravid obesity is an independent and strong risk factor for childhood overweight risk.

Identifying the mechanisms beyond the association of maternal pregravid obesity and GDM with offspring overweight is crucial in order to develop effective intervention/prevention strategies to interrupt the intergenerational vicious cycle.

WS.4: Horizon 2020 – EU Research and Innovation Programme

Saturday 15th March, 9.00-10.05

Horizon 2020: Research opportunities in the food sector for a safe and healthy diet

Isabelle de Froidmont-Görtz

Unit for Food, Health and Well-being, DG Research and Innovation, European Commission, BRUSSELS, BELGIUM

The aim of this symposium is to provide information on the new call for proposals for "Societal Challenge 2" (Food security; sustainable agriculture and forestry; marine, maritime and inland water research; and bio-based industries and the bioeconomy). Research and innovation opportunities will be discussed as valuable tools for fostering the sustainability and competitiveness of the European agri-food and seafood sectors and for promoting healthy and safe diets among Europe's citizens. Professor Berthold Koletzko (EARLY NUTRITION) and Cristina Campoy (NUTRIMENTHE), FP7 project coordinators will share their experience.

New Investigators Forum

Saturday 15th March, 9.00-10.05

Finding Spontaneous Preterm Birth biomarkers from metabolomics data when unknown subgroups exist.

Considine E.C., Kenny L.C., Khashan A., Holbrook J. A.
INFANT Centre, University College of Cork, CORK, IRELAND.

Metabolomics case control data from a highly heterogenous disease doesn't always benefit from typical metabolomics data analysis methods which search for a hyperplane or some other separator between cases and controls and designate biomarkers to be those features (metabolites) which contribute most to the separation between the 2 groups.
In the case of heterogenous diseases or states such as preterm birth where it is assumed that a variety of events/contributory factors/metabolomic states could possibly exist across an entire range of cases, a lower level analysis is required which examines the dataset more on a case by case and/or metabolite by metabolite basis.
However given that these datasets contain hundreds of thousands of datapoints this kind of detailed analysis has usually been eschewed in favour of a more high level approach which typically employs machine learning methods to train a classifier to separate cases from controls and in so doing identifies those features that contribute most to the separation between the two groups.
Using a dataset of 50 Spontaneous Preterm Birth cases and matched controls we searched for biomarkers in 3 different ways: using an arbitrarily defined healthy reference range based on controls; by investigating metabolite level change over time (15 weeks gestation to 20 weeks gestation) in cases vs controls, and in the traditional way by performing PLSDA and univariate analysis.)
In this way potentially informative metabolites that could predict the occurrence of Sponataneous Preterm Birth have been revealed that warrant further investigation and validation.

The Young Coeliacs of the PreventCD Study – A prospective cohort at high-risk for coeliac disease

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EU-PreventCD (www.preventcd.com) is a prospective double-blind intervention study investigating the effect of early gluten introduction on development of coeliac disease (CD) in high-risk children. This study is still blinded as to the effect of the intervention, and aims to characterize the development of CD in the PreventCD cohort at age 3y. From 2007-2010, 1324 infants with a 1st degree CD relative were recruited in 8 countries shortly after birth. Out of 944 included children, 772 have been followed clinically and serologically until 3y of age. Small bowel biopsies (SBBs) were performed based on CD suggestive symptoms, and/or anti-tissuetransglutaminase-antibodies (TG2A) or antigliadin-antibodies (AGA).
The cohort's mean age is 5.0y; 48.1% girls; 89% DQ2+; 55.8% were breastfed ≥6 months. Hundred-and-one SBBs were performed in 94 children. CD was confirmed by SBBs in 77 children and in 3 without SBBs. The cumulative incidence (CI) of CD at 3y was 5.2%. The mean age at diagnosis was 2.8y, 58.8% younger than 3y. All 80 children with CD had elevated TG2A. CD was not significantly associated with pregnancy duration, birth weight, duration of breastfeeding, or number/type of CD relatives. CD developed more frequently in girls (CI 7.2% vs. 3.4%; p=0.03), and in children homozygous for DQ2 (CI 14.9%) when compared to other HLA-risk groups (p <0.0001). These preliminary results show that genetically susceptible children from high-risk families develop CD very young and that this is significantly associated with DQ2-homozygosity. Even in very young children, presence of TG2A is a powerful predictor of CD.

Metabolic profiling of blood plasma in the field of early nutrition

EARLYNUTRITIONMEMBER

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Metabolic profiling can be described as the analysis of low molecular weight intermediates of a biological system. The current metabolic state of all living organisms including humans results from individual genetics, long-term environmental exposures and recent nutritional

intake. Blessing and curse, each of these factors are reflected to different extents in the metabolic profile of study subjects. Metabolic signatures have been described from various sample matrices, but blood plasma seems to be most useful in large scale human studies. Tissue samples are only available after highly invasive biopsies, which precludes their collection in large scale human observational studies. Urine and salvia as non-invasive samples are only suitable for water soluble metabolites or biomarkers, respectively, excluding the investigation of the whole field of lipidomics.
Untargeted analyses such as high-resolution mass spectrometry cover as many analytes as possible for the description of the whole complexity of a biological system. These techniques are strong for the characterization of completely unknown metabolic conditions and pathways. Targeted metabolic profiling, however, focuses on predefined metabolites from specific metabolic fields e.g. lipid metabolism. The limited number of analytes allows a more accurate identification and quantification and thus, comparisons between samples obtained in different metabolic states enable the understanding of alterations resulting from changes in the activity of metabolic pathways. Using bioinformatic tools and multivariate statistics relationships between metabolite concentrations and flux variations may be discovered. In the field of early nutrition, metabolic profiling supports the understanding of early programming effects of pre-pregnancy status, maternal nutrition, impaired placental transfer, duration of breastfeeding or the composition of infant formulas on anthropometric and developmental outcomes.

Maternal intake of vitamin A in mid-pregnancy and risk of child allergic disease – Results from the Danish National Birth Cohort

EARLYNUTRITIONMEMBER

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Background: Vitamin A has been shown to play an important role in early immunity and infections, but studies on prenatal vitamin A and child allergic disease are few and inconsistent.
Objective: To examine the relation between maternal intake of vitamin A from diet and supplements and child asthma and allergic rhinitis.
Methods: We used data from 44,594 mother-child pairs from the Danish National Birth Cohort. Maternal intake of vitamin A from diet and supplements was calculated based on information from a validated food frequency questionnaire completed around 25th week of gestation. At 18 months interviews with the mothers were used to evaluate doctor-diagnosed child asthma. At age 7, we assessed asthma and allergic rhinitis by the ISAAC questionnaire and by national registries on hospital diagnosis and medication use. Current asthma was defined by maternal report of asthma diagnosis and wheeze in the past 12 months. We calculated multivariable risk ratios and 95% confidence intervals for the associations of maternal vitamin A intake with child allergic disease.
Results: Maternal total vitamin A intake was not associated with child asthma. However, maternal vitamin A from diet was directly related to current asthma at age 7 (1.20, 95%CI: 1.03, 1.39 for 1000µg/day increase) and asthma medication use (1.04, 95%CI: 0.99, 1.09). There was a weak inverse association for maternal vitamin A with child allergic rhinitis, although not statistically significant.
Conclusion: Overall, maternal vitamin A intake does not appear to modify risk of child allergic disease, but the vitamin source and disease manifestation may be of importance.

I.Family Symposium: Health and Development of Small Children: Observations from the IDEFICS-I.Family Cohort

Saturday 15th March, 9.00-10.05

Pre- and perinatal influences on the weight status of primary school children

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The childhood obesity epidemic continues to be matter of concern despite increased public health awareness. Although weight loss and weight loss maintenance interventions remain the most used options at the individual and population levels, prevention strategies should be implemented to counteract the increase in body mass early in the life. In recent years, strong evidence in support of periconceptional, in utero and postnatal programming of offspring obesity has accumulated, whereby factors related to interaction between mother and foetus first, and nutrition practices in early infancy may play an important role. Accordingly, it has been suggested that the optimal time to prevent the development of overweight and obesity during childhood would be the pregnancy itself, along with the feeding strategies during the first six month of life. A number of players concurs in altering adiposity in the foetus and in the newborn, possibly inducing long-term changes which predispose the offspring not only to excess body weight but also to insulin resistance and other metabolic abnormalities later in the life. A better understanding of these processes may provide opportunities for the prevention of obesity and improved public health. In the framework of the IDEFICS and I.Family projects, we analysed information, collected from one of the largest European cohorts of preschool/school children that may contribute to answer these research questions. Several pre-, peri- and post-natal conditions were investigated -including gestational weight gain, weight of the child at birth, exposure to different infant feeding practices- to assess their contribution to excess body mass.

Ethical issues in large-cohort research: social relevance and distributed responsibilities

Garrath Williams, on behalf of the IDEFICS and I.Family consortia

Dept. of Politics, Philosophy and Religion, Lancaster University, LANCASTER, UK

What responsibilities do we have, as scientists conducting large-scale epidemiological research, to ensure that our work is relevant to the policy domain? What efforts should we make that our findings are taken up by other actors in society? Here, I suggest that two competing imperatives are relevant, taking examples from the research pursued in the I.Family study and the approach we took to ethical questions in our previous IDEFICS study. First, there is an ethical imperative to pursue research for the sake of social goods. The deployment of significant resources and the use of many participants' time and energy over an extended period suggest that scientists bear a responsibility to address issues of social significance. Obviously, research regarding human health fulfils this criterion, even though the relevance of many findings is likely to become clear only later. This imperative to promote social goods implies a wider duty to ensure the exploitation of research. The second imperative then follows from this, but is more complex and permits much contestation in practice. Beyond the responsible publication of research findings there is a wider imperative to act on those. However, this imperative is a social duty and as such can only be fulfilled by the cooperation of many actors with many responsibilities where clarifying the relevance of our findings to different actors represents a shared responsibility. As such, we should be hesitant to assume that even quite clear research findings have immediate implications for action, whether at the policy level or regarding individual or parental responsibilities.

Expected future insights from the I.Family study

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Many factors are at play today that make it difficult to choose the lifestyles that will help maintain health and well-being. The living environment, social conditions, economic pressures and family lifestyles have changed over recent decades. Often both parents are working and the time spent together with their children is limited. Self-prepared meals from local ingredients are replaced by fast and ready-made foods. Concerns about safety on streets, limited availability of play spaces, exposure to TV and increased time playing computer games have pushed physical activity out of the daily lives of young people. These changes profoundly impact children's health, particularly those in the most vulnerable groups. More and more are obese, experience metabolic disorders and are affected by psychological problems. Many of these disorders track into adulthood.

The I.Family study wants to unravel the factors at play and their complex interplay, to identify effective interventions and to support policy development, enabling more families to make healthier choices. For this purpose, the I.Family study builds on the IDEFICS cohort established in 2007 with more than 16.000 children recruited from eight European countries aged 2 to 9 years at the first examination. Some of the children are now experiencing changes around puberty, as they are in the transition between childhood and adulthood. Even if children have developed healthy eating and activity patterns, their lives change considerably as they become teenagers. Healthy routines can easily be lost and replaced by unhealthier habits, perhaps because of the influence of marketing or peer pressure.

I - Prevention and Intervention

I-1 Higher protein intake in infancy is associated with increased visceral fat at 5 years of age

EARLYNUTRITIONMEMBER **Poster of Distinction**

Gruszfeld D.[1], Socha P.[1], Gradowska K.[1], Martin F.[2], Weber M.[3], Verduci E.[4], Closa-Monasterolo R.[5], Koletzko B.[3], CHOP Study Group

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Background: The European Childhood Obesity Project (CHOP) demonstrated that higher protein content in infant formula increases body mass index (BMI) at 2 years of age. Compared to BMI the measurement of visceral fat may provide a better understanding of metabolic risks associated to variations in fat distribution.

We examined the effect of different protein intake in infancy on the amount of preperitoneal (PP) and subcutaneous (SC) fat measured by ultrasound at the age of 5 years.

Methods: The CHOP study is a multicenter, randomized clinical intervention trial examining the effect of early protein intake on later obesity risk.

Healthy term formula fed infants in five European countries were randomized either to higher (HP) or lower (LP) protein formula in the first year of life and at least three months long breastfed (BF) infants were enrolled as an observational group. SC and PP fat were measured in 274 children participating in the follow-up examination at the age of 5 years. Log-transformed values were used for analysis in linear regression models.

Results: The PP fat layer was significantly thicker in the HP group (median area 0.43 cm2 [IQR 0.32-0.54 cm2]) than in the LP group (0.36 cm2 [IQR 0.27-0.47 cm2], adjusted estimated difference 0.138 [95%CI 0.024-0.251] p=0.018) and BF group. In contrast, there was no difference between the HP an LP group in SC fat.

Conclusion: Higher protein intake in infancy is associated with an increased amount of visceral fat tissue but not with subcutaneous fat tissue in later childhood.

I-2 Neonatal leptin administration improves cognitive impairment in a rat model of postnatal growth restriction

Poster of Distinction

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Postnatal growth restriction (PGR) is associated with impaired neurodevelopment, and lower serum leptin in preterm infants. We have demonstrated the same in a rodent model. As leptin is important in CNS myelination, we hypothesized that leptin is causally related to poorer neurodevelopment in PGR. Using our previous model, newborn rats were randomized to litters of 10/dam (N, Normal, n=70) or 18/dam (PGR, n=108) until weaning (d21). Between d8-14, half the pups in each litter were randomized to 3 ug/kg/d rat leptin s.c., half to PBS. After weaning, a high-fat rodent chow was fed ad libitum to d75. All rats had glucose tolerance and insulin stimulation tests, as well as cognition (spontaneous alternation in a T-maze) assessed. PGR rats were 30% smaller than N rats from d5-21 ($p< 0.0001$). Female PGR rats caught-up with N rats by d75, but male PGR rats remained 15% smaller. Leptin administration increased serum leptin levels but did not affect growth. In PBS-treated rats, neurodevelopment was worse in PGR (5.5 ±1.2) than N rats (7.0 ±0.8, $p< 0.0001$). Leptin improved neurodevelopment in PGR (7.0 ±1.0, $p< 0.0001$) but not N rats (7.2 ±1.2, p=NS). PGR rats had improved glucose tolerance (p=0.015) and insulin sensitivity (p=0.0001), but leptin had no effect. Leptin reversed cognitive impairment in rats with PGR, without adverse effects on growth, insulin sensitivity, or glucose tolerance. This model and findings merit further investigation in preterm infants.

I-3 Maternal dietary supplementation with specific non-digestible oligosaccharides leads to reduced allergic asthma symptoms in their offspring

Poster of Distinction

Hogenkamp A.[1], Thijssen S.[1], van Vlies N.[1], Knippels L.[1,2], Garssen J.[1,2]

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Maternal supplementation with non-digestible carbohydrates may beneficially affect maternal and fetal immune status in mice. We investigated whether maternal supplementation during pregnancy leads to long-term programming of the immune system in the offspring. To this end, immune responses in the offspring were studied in an ovalbumin (OVA)-induced model for experimental allergic asthma.

Female mice were fed a control diet or a diet supplemented with short-chain galacto- and long-chain fructo-oligosaccharides (scGOS/lcFOS; ratio 9:1). After 2 weeks, mice were mated. All dams were transferred to control diet after birth of the offspring. Male offspring were sensitized to OVA at 6 weeks, and the acute allergic skin response was measured at 8 weeks. The offspring were challenged 3 times with nebulized OVA, after which lung function was measured.

In offspring of dams supplemented with scGOS/lcFOS (scGOS/lcFOS-group), the acute allergic skin response was reduced compared to the offspring of dams fed the control diet (control-group). Correspondingly, a dramatic decrease in lungresistance was seen in scGOS/lcFOS-group. Furthermore, whereas IgE levels were elevated in the control group, no such increase was observed for the scGOS/lcFOS-group. IgG2a levels were significantly higher in the latter group compared to the other experimental groups, and a significant increase in the percentage of regulatory T cells in the spleen was observed.

In conclusion, maternal supplementation with a specific mixture of oligosaccharides during pregnancy leads to a significant decrease in allergic symptoms in the offspring, suggesting a beneficial programming effect. Results from this study indicate a role for regulatory T cells.

I-4 The effect of antenatal dietary and lifestyle advice on fetal body composition in women who are overweight or obese: findings from the LIMIT randomised trial

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Objectives: Overweight and obesity are recognized risk factors for fetal growth disturbances, with associated maternal and fetal risks. We aimed to assess the effect of an antenatal dietary and lifestyle intervention on fetal body composition at 28 and 36 weeks gestation.
Methods: We conducted a randomised controlled trial evaluating the effect of a dietary and lifestyle intervention for women who were overweight or obese during pregnancy on maternal and infant health outcomes. Women were eligible for the LIMIT trial with a BMI ≥ 25kg/m², and a live singleton pregnancy. Fetal body composition (mid thigh lean (MTLM) and fat mass (MTFM), abdominal fat mass (AFM) and subscapular fat mass (SSFM)) were assessed prospectively using ultrasound at 28 and 36 weeks' gestation. Ultrasound measurements were analysed using linear mixed effects models, with adjustment for potential confounding factors. Statistical significance was assessed at the 2-sided p< 0.05 level. All analyses were performed using SAS v9.3 (Cary, NC, USA).
Results: Of women who consented to the LIMIT trial, 78 % attended for a research ultrasound at 28 (1733 scans) and 36 weeks (1713 scans) gestation. An antenatal dietary and lifestyle intervention resulted in a reduction in growth of SSFM measures between 28 and 36 weeks. There were no other differences identified for the remainder of body composition measures at either 28 or 36 weeks.
Conclusions: An antenatal dietary and lifestyle intervention modifies fetal fat mass deposition, as evidenced by findings from this large randomised controlled trial.

I-5 Offspring of ovalbumin-sensitized mice supplemented with specific non-digestible oligosaccharides during pregnancy or lactation display attenuated allergic responses in a model for Hen's Egg food allergy

Poster of Distinction

Hogenkamp A.[1], van Esch B.[1], Knippels L.[1,2], Garssen J.[1,2]

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Non-digestible carbohydrates have beneficial effects in infants and young children, but not much is known about their effects during pregnancy or lactation. We investigated whether maternal supplementation could have long-term programming effects on immune responses in the offspring of both sensitized and non-sensitized dams.
Female mice were sensitized orally to ovalbumin (OVA) using cholera toxin (CT) as adjuvant. Control groups received CT. Two weeks after the last sensitization mice were mated and fed either a control diet or a specific non-digestible oligosaccharide mixture containing shortchain-Galacto-, longchain-Fructo- and Acidic-oligosaccharides (9:1:1) (scGOS/lcFOS/pAOS) during pregnancy or lactation. After weaning, female offspring were fed control diet and sensitized to OVA. One week after the last sensitization, the offspring were challenged intradermally with OVA, and the acute allergic skin response was measured.
Acute allergic skin responses in the offspring of scGOS/lcFOS/pAOS supplemented OVA-sensitized dams (OVA-scGOS/lcFOS/pAOS groups) was significantly reduced compared to offspring of OVA-sensitized mice fed the control diet throughout pregnancy and lactation. In contrast, supplementation did not significantly attenuate the acute allergic skin response in the CT-scGOS/lcFOS/pAOS groups. In the OVA-scGOS/lcFOS/pAOS-lactation group, OVA-specific Ig-levels corresponded with these effects, but supplementation of OVA-sensitized dams during pregnancy does not appear to affect Ig-levels. In the offspring of non-sensitized dams similar effects could be observed, but the results are less clear.
In conclusion, maternal supplementation with specific mixture of non-digestible carbohydrates significantly reduced the allergic skin response in the offspring of OVA-sensitized dams, indicating a beneficial programming effect on the immune response.

I-6 Role of slow digesting carbohydrates during pregnancy for improving insulin sensitivity in offspring of obese rats. (NIGOhealth study)

EARLYNUTRITIONMEMBER

Poster of Distinction

Lopez-Pedrosa J.M.[1], Bueno P.[1], Manzano M.[1], Martin M.-J.[1], Giron M.-D.[2], Salto R.[2], Vilchez J.D.[2], Cabrera E.[2], Rueda R.[1]

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Maternal obesity is known to increase the risk of developing metabolic syndrome by the offspring. We examined the effects of two mixtures of carbohydrates (CHO) consumed by pregnant rats, exposed to high fat diet, on insulin sensitivity in the adolescent offspring. Virgin rats were fed a high fat 6 weeks before mating and then fed a HF diet containing either CHO with high (HF/HC) or low (HF/LC) digestion rate throughout pregnancy. Control rats received AIN93G diet. At delivery all the animals were fed standard rodent diet (13 weeks). Plasma glucose was analyzed by PENTRA, and insulin using Luminex technology (Bioplex). Muscle and adipose GLUT4 and Akt were assayed by Western blot.
Slow digesting CHO were able to revert the deleterious effects of high fat diet exposure in uterus by keeping Akt and GLUT4 expression at normal levels, and thus insulin-dependent glucose uptake was similar to control and higher than that of HF/HC rats. Both plasma glucose and insulin levels were lower in HC/LC offspring when compared to both control and HF/HC offspring. Furthermore, in this group insulin sensitivity (ISI-Mat) was higher as compared with HF/HC rats.
These data further reinforce the importance of maternal nutrition during gestation and show that a slow digesting carbohydrate in maternal diet has the potential to influence offspring metabolism preventing the susceptibility to develop insulin resistance.

I-8 Paternal consumption of a lard but not corn oil-based high fat diet programmed breast cancer susceptibility in the female offspring

Poster of Distinction

Fontelles C.C.[1], Guido L.N.[1], Rosim M.P.[1], Andrade F.D.O.[1], de Assis S.[2], Hilakivi-Clarke L.[2], Ong T.P.[1]

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The present study investigated whether paternal consumption of high fat diets increases breast cancer susceptibility in female offspring. Male rats (n=20/group) consumed a lard-based (LB) high fat diet (60% of fat-derived energy), corn oil-based (CB) high fat diet (60% of fat-derived energy) or AIN-93G control (CON) diet (16% of fat-derived energy) for 9 weeks during the development and sexual maturation periods. They were mated with female rats (1 female per male rat) consuming a regular commercial diet. Their 7-week-old female offspring were exposed to 7,12-dimethyl-benza[a]anthracene to induce mammary tumors. Male rats consuming these high fat diets (LB and CB) showed higher fasting glycaemia (p< 0.05) and body fat relative weight (p< 0.05) compared to male rats consuming the CON diet. 50-day-old LB female offspring showed higher body weight (p=0.02) and fasting glycaemia (p=0.01) compared to 50-day-old CON

and CB female offspring, respectively. There were no differences (p>0.05) between CON and CB female offspring regarding these parameters. 50-day-old CB, but not LB, female offspring showed higher (p=0.02) retroperitoneal fat relative weight compared to 50-day-old CON female offspring. LB female offspring showed higher (p< 0.05) incidence of palpable mammary tumors compared to CB and CON female offspring. There were no differences (p>0.05) between CON and CB female offspring regarding this parameter. Additionally CB offspring showed higher (p=0.01) first tumor latency compared to LB offspring. Our data show that paternal high fat consumption can programme female offspring's susceptibility to breast cancer and that these effects are dependent on the fatty acid profile.

I-9 Role of slow digesting carbohydrates during pregnancy for preventing adiposity programming in offspring of obese rats. (NIGOhealth study)

EARLYNUTRITIONMEMBER **Poster of Distinction**

Lopez-Pedrosa J.M.[1], Martin M.-J.[1], Manzano M.[1], Bueno P.[1], Giron M.-D.[2], Salto R.[2], Vilchez J.[2], Cabrera E.[2], Rueda R.[1]

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Maternal obesity is known to increase the risk of developing metabolic syndrome by the offspring. We examined the effects of two mixtures of carbohydrates (CHO) consumed by pregnant rats, exposed to high fat diet, on body adiposity either in the pregnant mothers or in the offspring. Virgin rats were fed a high fat 6 weeks before mating and then fed a HF diet containing either CHO with high (HF/HC) or low (HF/LC) digestion rate throughout pregnancy. Control rats received AIN93G diet. At delivery all the animals were fed standard rodent diet (13 weeks). Body composition was analyzed longitudinally by using MRI. Proteins key to metabolic flux in white adipose tissue were assayed by western blot.

HF/HC dams had significant lower body weight gain compared to C and HF/LC dams. HF/HC offspring had significantly higher fat mass accretion than the C offspring group (t-test; p< 0.05). In contrast, HF/LC offspring exhibited similar adiposity to control. Phosphoenolpyruvate carboxykinase amount was higher in HF/HC as well as both acetylCoA carboxylase and pyruvate carboxylase, pointing out that glycerogenesis and fatty acid synthesis cascades were stimulated leading to an enhanced deposition of lipids in the adipose tissue. Altering the carbohydrate profile of maternal diet during gestation has the potential to program metabolism in offspring by modifying the rate of lipogenesis in the white adipose tissue.

*The research leading to these results is part of the European Union´s Seventh Framework Programme (FP7/2007-2013), project EarlyNutrition under grant agreement n°289346

I-10 Effects of exercising obese pregnant mice on their hepatic metabolic profile

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Background: Obesogenic diets during pregnancy alter the intrauterine environment and the metabolic phenotype of the adult offspring. These diets also change hepatic lipid metabolism in association with increased adiposity in pregnant mouse dams (Musial et al, DOHaD 2013). This study examined the effects of exercising before and during pregnancy on hepatic lipid metabolism of obese dams near term.

Methods: C57BL6 female mice were fed either a control diet (n=6) or a diet that induced obesity (n=12). Five of the obese group were then exercised (20 min/day, 5 days/week) for a week before mating until day(D) 17 of a 20.5D pregnancy. After euthanasia at D19, maternal liver was collected, weighed and snap frozen. Hepatic fat content and selected markers of lipid metabolism were measured by Folch extraction and Western blotting, respectively. Statistical significance was assessed by 1-way ANOVA with multiple comparisons.

Results: In obese dams, exercising reduced the lipogenic fatty acid synthase and normalised the elevated sterol regulatory element binding protein abundance to control values (P< 0.05, both cases). Exercising obese dams also tended to further increase fatty acid transport protein 1 and to reduce proliferator peroxisome activated receptor γ, lipoprotein lipase and fat content towards control values, although none of these changes were statistically significant.

Conclusion: Exercising obese mouse dams reduced hepatic markers of fat synthesis coupled with a tendency for decreased fat storage. This may contribute to the improved glucose tolerance seen in the exercised obese dams in late pregnancy (Fernandez-Twinn et al., 2014, this meeting).

I-12 Maternal n-3 polyunsaturated fatty acid status in late pregnancy and neonatal body composition: Growing Up in Singapore Towards healthy Outcomes (GUSTO)

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Introduction: Maternal n-3 polyunsaturated fatty acid (PUFA) status, especially long chain n-3 PUFA, has been associated with lower adiposity in offspring, but the evidence is inconclusive. We aim to further elucidate this association in an Asian population.

Methods: The GUSTO birth cohort study comprises mothers (n=1152) with a mean age of 30.4 years and ethnic composition of 54% Chinese, 27% Malays, and 18% Indians. Maternal plasma samples (n=999) collected during 26th-28th week gestation were assayed for fatty acid profile. Neonatal anthropometric measures of body fatness (BMI, ponderal index, abdominal circumference, subscapular and triceps skinfolds) were determined within 72 hours after birth.

Results: After adjustment for potential confounders (maternal, socio-economic, and child factors), total n-3 PUFA (% of total fatty acid) and n-3 to n-6 PUFA ratio were not significantly associated with the studied outcome measures. However, among individual n-3 PUFA, higher α-linolenic acid (ALA, 18:3n-3) was significantly associated with lower triceps skinfold (β= -0.13 mm per SD increase; 95% CI: -0.21 to -0.06). In addition, eicosatetraenoic acid (ETA, 20:4n-3) was associated with lower triceps skinfold (β= -0.11 mm; -0.19 to -0.03) and lower subscapular skinfold (β= -0.09 mm; -0.16 to -0.02). In contrast, the long-chain n-3 PUFA eicosapentaenoic acid (EPA, 20:5n-3), docosahexaenoic acid (DHA, 22:6n-3), and docosapentaenoic acid (DPA 22:5n-3) were not significantly associated with the studied measures of body fatness.
Conclusions: Our results suggest that the less well-studied n-3 PUFA- ALA (shorter chain) and ETA (long chain) may be associated with lower neonatal adiposity indicated by lower skinfold thickness measurements.

I-13 The adipogenic lipidome of obese rat offspring is reversed by slow digesting carbohydrate diets during pregnancy. NIGOhealth study

EARLYNUTRITIONMEMBER

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Maternal obesity is known to increase the risk of developing metabolic syndrome by the offspring. We examined the effects of two mixtures of carbohydrates (CHO) consumed by pregnant rats, exposed to high fat diet,on the offspring lipidomics signature.
Virgin rats were assigned to three experimental groups: control (C) dams fed a standard rodent diet before mating and throughout pregnancy; dams fed a high fat diet (HF) 6 weeks before mating and then fed a HF diet containing either CHO with high (HF/HC) or low (HF/LC) digestion rate throughout pregnancy. At delivery, all the animals were fed the standard rodent diet for the remainder of the study (13 weeks). Offspring were subjected to plasma and renal adipose tissue lipidomics studies. More than 180 lipid species were analysed reverse ultra-performance liquid chromatography coupled to mass spectrometry (UPLC-MS).
HF/HC adolescent offspring presented increased adiposity than the HF/LC and the C offspring groups. This finding was highlighted by the enlarged concentration of diverse lipid species in the HF/HC plasma, such as medium-chain triglycerides, phosphatidylcholines and lysophospholipids. HF/HC and HF/LC exhibited completely different adipose and plasma lipid profiles when compared to C. Interestingly, a number of triglycerides decreased very profoundly in HF/LC offspring while they followed an upward trend in HF/HC and in controls. Slow digesting carbohydrate diets during gestation prevent adipogenic lipidome in the progeny.
*The research leading to these results is part of the European Union´s Seventh Framework Programme (FP7/2007-2013), project EarlyNutrition under grant agreement n°289346

I-14 Interaction of pre-conceptional food supplementation with maternal BMI: Reduces gestational diabetes in undernourished women and increases birthweight in well-nourished women

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Background: Mumbai Maternal Nutrition Project was a food based Randomized Controlled Trial, aimed to assess whether pre-conceptional micronutrient supplementation is associated with improved fetal growth. The intervention was a daily snack made from Green Leafy Vegetables, fruit and milk, prior to conception and throughout pregnancy. Control supplements contained foods of low micronutrient content.
Method: The trial was conducted in Mumbai slums between 2006 and 2012. Married non-pregnant women aged < 40 years were recruited following written informed consent. They were randomised to receive supplements daily under supervision. During pregnancy an oral glucose tolerance test was carried out (median 29 weeks). Gestational diabetes (GDM) was defined as a fasting glucose >7 mmol/l or 120-minute glucose >7.8 mmol/l. Birth weight was measured by trained staff within 72 hrs of delivery.
Results: 6,513 non-pregnant women were enrolled (mean age 24 years and BMI 20). Baseline characteristics were similar except that control women had larger waist circumference (+0.6 cm, p=0.05).
Intervention increased birth weight by 48g overall (control: 2583g, treatment: 2631g; p=0.05). The effect increased with increasing maternal BMI (+113g, p=0.008; +79g, p=0.07 and -8g, p=0.8 in the highest, middle and lowest thirds of maternal BMI. The prevalence of GDM reduced in the intervention group (Intervention: 7.5% vs Control: 13.3%; p=0.01), predominantly among thinner women (BMI < 22).
Conclusion: Differential effect of maternal BMI is seen in women, where daily consumption of micronutrient-rich snack reduce incidence of GDM in undernourished women but increased birthweight in well nourished women.

I-15 Auditory evoked fetal brain activity is affected by insulin sensitivity of the mother

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Aims: Fetal programming plays an important role in the pathogenesis of type 2 diabetes. Our aim was to investigate whether maternal metabolic changes during OGTT (oral glucose tolerance test) influence fetal brain activity.
Methods: Thirteen healthy pregnant women underwent an OGTT (75g). Insulin sensitivity was determined by glucose and insulin measurements at 0, 60 and 120 minutes. At each time-point fetal auditory evoked fields were recorded with a fetal magnetoencephalographic device, response latencies were determined.

Results: Sixty minutes after glucose ingestion, insulin increased from 67 ± 25 (Mean ± Standard Deviation) to 918 ± 492 pmol/l and glucose levels from 4.4 ± 0.3 to 7.4 ± 1.1mmol/l. Fetal response latencies decreased between 0 and 60 minutes from 297 ± 99 to 235 ± 84ms (p=0.01) and remained stable until 120 minutes (235 ± 84 vs. 251± 91, p=0.39). There was a negative correlation between maternal insulin sensitivity and fetal response latencies 60 minutes after glucose ingestion (r=0.68, p=0.02). After a median split of the group based on maternal insulin sensitivity, fetuses of insulin resistant mothers showed a slower response to auditory stimuli (283 ± 79ms) compared to fetuses of insulin sensitive mothers (178 ± 46ms, p=0.03).
Conclusions: Lower maternal insulin sensitivity is associated with slower fetal brain responses. These findings provide first evidence that maternal metabolism has a direct effect on fetal brain activity and suggest that central insulin resistance may be programmed during fetal development.

I-16 Effects of Maternal Hyperglycemia at Different Stages of Gestation on Male Reproductive Functions in Rats

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Infants of hyperglycemic mothers may develop a myriad of metabolic disorders early in adult life. It is however not known if there are consequences on their reproductive functions. The relationship between maternal hyperglycemia and reproductive function of male offspring was investigated. A single intraperitoneal injection of alloxan (90mg/kg body weight) was used to achieve maternal hyperglycemia at different gestational days (GD1, GD8 and GD15). The animals were subsequently given 10% glucose daily in drinking water. The following were assessed: birth weight, Anogenital Distance (AGD) index, testes descent day, preputial separation day, seminal profile; serum levels of reproductive hormones; and the weight and histology of the testis and epididymis. GD1-21 pups showed a significant increase in mean birth weight and AGD index ($p< 0.01$) as compared to control. GD8-21 pups showed a significant decrease in mean birth weight ($p< 0.01$). Testes descent day and preputial separation day in all the experimental groups was significantly decreased. There was a significant reduction in sperm count and viability in GD8-21 ($p< 0.01$). Sperm motility was significantly reduced in all test groups. Histological sections of the testis and epididymis of all test groups showed thickened tunica propria and vascular congestion. It is deduced from this study that maternal hyperglycemia (especially during GD8-21) caused alterations in reproductive functions in male offspring of albino rats.

I-17 Maternal dairy calcium supplementation reduces adiposity in offspring´s

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Introduction: Role of calcium in preventing adiposity is known in single generation studies, but remains unexplored in inter-generational set-up. In that case it will highlight its role in early programming of risk for non-communicable diseases. We examined the impact of maternal calcium supplementation on adiposity in adult offspring's of wistar rats.
Methods: Pregnant dams (n=8/group) randomly received AIN-93G diets either with control (C-0.5% $CaCO_3$) or high inorganic (CaS-1.2% $CaCO_3$) or high dairy calcium (CaD- 1.2% from non-fat dairy milk) throughout gestation. Pup's whole and regional body fat was measured at 90 days using non-invasive Dual X-ray absorptiometry technique.
Results: Pre-pregnancy dam weights, length of gestation and birth weights of pups were comparable in control and experimental groups. At 90 days, body fat percent in pups from CaD group was significantly ($p< 0.05$) low compared to those from CaS and C groups (Males- 2.2% Vs 2.6% and 3.2%; Females- 2.6% Vs 4.3% and 5.2%). More importantly, the differences were significant for body fat percent in abdominal region (Males 0.7% Vs 0.9% and 1.2%; Females 0.9% Vs 1.6% and 2.2%). Thus, impact of dairy calcium was more prominent compared to inorganic calcium confirming the earlier observations in single generation studies.
Conclusions: The findings highlight the role of dairy calcium in modulating adiposity, especially in visceral region in offspring's. As visceral fat is known to be a major risk factor for metabolic syndrome, the observations underscore role of calcium in early programming.

I-18 Maternal vitamin D status in pregnancy and offspring bone health: A systematic review and meta-analysis

EARLYNUTRITIONMEMBER

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Aim: To elucidate the role of vitamin D in pregnancy in maternal and offspring health.
Methods: Major electronic databases were searched from inception till June 2012, together with hand-searching of bibliographies and author contact. Primary outcomes: Maternal osteomalacia; Neonatal hypocalcaemia, rickets and bone mass. Secondary outcomes: Maternal quality of life; Neonatal body composition and bone mass, later offspring health (including asthma, diabetes, immune disease). We performed systematic review and where possible meta-analysis. All assessments were performed by two reviewers and according to UK CRD guidance.
Results: After screening of 16,841 citations, 172 remained, with 73 finally included (including 10 clinical trials). There was considerable heterogeneity between the studies and for most outcomes there was conflicting evidence; however modest positive relationships were found between maternal serum 25(OH)D and 1) offspring birth weight in meta-analysis of 3 observational studies; 2) offspring cord blood or postnatal calcium concentrations in a meta-analysis of 6 intervention studies (all found to be at high risk of bias); and 3) offspring bone mass in 5 observational studies felt to be of good quality, but which did not permit meta-analysis.
Conclusions: Although there was weak evidence to support a relationship between maternal 25(OH)-vitamin D status and offspring birth weight, bone mass and serum calcium concentrations, these findings were limited by their observational nature or low quality and

risk of bias. High-quality intervention studies to investigate these outcomes would be appropriate, but the current evidence base is insufficient to directly inform clinical practice.

I-19 Later taste preferences of rats raised on hydrolysate formula

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Most of protein hydrolysate formula are rich in free amino acids and have particular flavor of amino acids. We examined the impact of hydrolysate formula-feeding in infancy on the taste preferences after weaning using our rat artificial rearing systems. Rats were fed commercial standard infant formula, whey hydrolysate formula, or casein hydrolysate formula with a formula-feeding bottle for rats during the daytime and fed milk formula for rats through a intragastric catheter during the night-time from 9 to 20 days of age. Other rats were raised on the casein hydrolysate formula by means of a formula-feeding device for rats from10 to 20 days of age. All rats were fed a standard solid diet after 20 days of age. Taste prefereces of each rat to leucine and glutamate were evaluated by two bottle preference tests at 7 and 10 weeks of age. At 7 weeks of age, dam-fed rats, standard formula-fed rats, and whey hydrolysate formula-fed rats prefered leucine or glutamate solution against water, whereas the prefereces of two casein hydrolysate formula-fed groups were significantly low compared with the dam-fed rats, and the preference rates were close to 50%. At 10 weeks of age, threre was no significant difference in preference of amino acid solutions among the groups. Our results suggest that feeding of hydrolysate formula in infancy may modify taste preferences and the modification could persist for a long while after weaning. Our rat artificial rearing systems may be usuful to investigate this issue.

I-20 Preconceptual nutrition and weight gain in a) women during pregnancy and b) in babies at birth in Mumbai Maternal Nutrition Project (a RCT)

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Mumbai Maternal Nutrition Project (MMNP), (2006 - 2012), was a food based Randomised Controlled Trial (RCT) in slum women to determine the effect of a daily snack made from green leafy vegetables (GLVs), fruit and milk, taken for at least three months before conception and until delivery, on birth weight at birth. Out of a total of 6513, 2310 women became pregnant and 1562 delivered singleton newborns.1094 newborns were measured.

Preconceptual Nutrition in Weight Gain of women during Pregnancy and babies born in MMNP trial is presented.

Results:

Women: Percentage of women gaining weight from Preconception to 28 weeks of gestation against their BMI levels (WHO) showed that:

1. Proportion of underweight women was reduced significantly from 34.5% to 5.6 % between pre conceptual and 28 weeks. (p =.001)
2. Proportion of overweight women was increased significantly from 9.7% to 25.9 % between pre conceptual and 28 weeks. (p =.001)
3. In women with normal BMI, percentage of women with weight gain remained constant between pre conceptual and 28 weeks.

Babies: Overall birth weight increased by 48 g (control:2583g,treatment:2631g; p =0.05). With reference to maternal BMI at preconception, this effect was best in the highest (>21.8) (+113g; p =0.008) and middle (18.6-21.8) (+79g, p =0.07) groups and nil (- 8g, p =0.8) in the lowest thirds (< 18.6). (p for interaction =0.001).

Conclusion: Pre conceptual BMI is a significant factor in determination of weight gain during the pregnancy and newborn weight in Indian slum women.

I-21 Human milk fatty acid composition and anthropometrical outcomes in infants during the first twelve months of life

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Background: The polyunsaturated fatty acids (PUFAs) content in human milk, especially docosahexaenoic and eicosapentaenoic acids (DHA+EPA) as well as n–6/n–3 PUFAs ratio were not often associated with infant's growth, which could be in fact the case. We studied the extent to which human milk fatty acid composition was associated with anthropometric measurements of infants in the first twelve months of their lives.

Design: Healthy pregnant women and their infants (n=87 mother-infant pairs) were included in the "My Milk" (www.moje-mleko.si/en) project registered at ClinicalTrials.gov (NCT01548313). We determined fatty acid composition (weight percent; wt. %) of mature human milk (equal mixture of fore- and hind-milk at one month after delivery) and took anthropometric measurements (body mass, length, head circumference, triceps, subscapular and front thigh skinfold thicknesses) of infants at one and twelve months. With t-test we examined the relative changes of infants´ anthropometric characteristic up to twelve months according to DHA+EPA content (cut of point set at 0.3 wt. %) and n–6/n–3 PUFAs ratio (cut of point set at 13) in human milk.

Results: Human milk DHA+EPA content was 0.33 (±0.21) wt. % (mean (±SD)), the n–6/n–3 PUFAs ratio was 13.84 (±4.66). DHA+EPA content had no effect on infant's growth velocity. Infants body mass (P=0.012) and length (P=0.010) up to twelve months increased slower in a group with higher n-6/n-3 ratio.

Conclusion: DHA+EPA content (wt. %) in human milk did not affect infants´ growth velocity, whereas higher n–6/n–3 PUFAs ratio decreased infants´ growth velocity during the first twelve months of life.

I-22 The association of maternal characteristics and macronutrient intake in pregnancy with neonatal body composition

EARLYNUTRITIONMEMBER

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Background: The in utero environment has been found to affect foetal development however many of the mechanisms by which this occurs remain unknown. Paediatric central adiposity has been found to be associated with metabolic syndrome in later life. The aim of this study was to examine the association between dietary macronutrient intake and lifestyle in pregnancy and neonatal body composition.
Methods: This was an analysis of 749 infants from the ROLO study (Randomised cOntrol trial of LOw glycaemic index diet versus no dietary intervention to prevent recurrence of fetal macrosomia). Food diaries as well as food frequency and lifestyle questionnaires were completed during pregnancy. Maternal anthropometry was measured throughout pregnancy and neonatal anthropometry was measured at birth.
Results: Multiple linear regression analysis revealed the main maternal factor associated with increased birth weight was greater gestational weight gain R2adj23.3% (F=11.547, p< 0.001). The main maternal factor associated with increased birth length was non-smoking status R2adj27.8% (F=6.193, p< 0.001). Central adiposity determined using waist:height ratio was negatively associated with maternal age, and positively associated with smoking status, pre-pregnancy mother arm circumference, percentage energy from saturated fat in trimester 3, trimester 2 glycaemic load, glucose challenge test and membership of the control group R2adj 38.1% (F=8.000, p< 0.001).
Conclusions: Several maternal diet and lifestyle factors were associated with neonatal body composition. The finding that central adiposity was positively associated with maternal dietary fat intake and membership of the control group highlights the importance of diet in pregnancy and the need for education in this area.

I-23 Impact of maternal hyperlipidic hypercholesterolemic diet on male reproductive organs and testosterone concentration in rabbits

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The concept of Developmental Origins of Health and Disease (DOHAD) has expanded for two decades. Many epidemiological studies and experiments in animal models have highlighted an increased risk of long-term metabolic and cardiovascular diseases in case of nutritional imbalance during pregnancy or gestation. Reproductive functions and fertility in adulthood may also be programmed during fetal development.
The rabbit is a relevant model to assess effect of developmental programming on reproductive functions. In our laboratory, a model of female rabbits fed with a diet enriched 6% of soybean oil and 0.2% cholesterol (HH) before and during pregnancy induced an intrauterine growth retardation and a metabolic syndrome in offspring at adulthood.
In this study, we studied the impact of HH diet, administered at 10 weeks of age and throughout the gestation and lactation, on male reproductive functions of rabbit offspring.
Rabbits born from HH dams had significantly lighter testes (p< 0,05) and epididymes (p< 0,05) compared to rabbits born from control dams. Considering the relative weight, the difference remained significant (p< 0,05 et p< 0,01 respectively). The seminiferous epithelium height was comparable between the 2 groups. No significant differences in sperm concentration, sperm DNA integrity and sperm membrane composition were observed. Interestingly, plasma free testosterone concentrations were decreased in males born from HH dams (p=0.05) at 37 weeks of age.
This study confirms the importance of maternal metabolic status and early environment for male reproductive organs development.

I-24 Probiotics in obese pregnancy to reduce maternal fasting glucose: A randomized controlled trial

EARLYNUTRITIONMEMBER

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Objectives: Probiotics are live microorganisms which may confer health benefits on the host. Recent studies have demonstrated various beneficial effects of probiotics in pregnancy among healthy women. The aim of this study was to investigate the effects of a probiotic capsule on maternal fasting glucose and pregnancy outcome in obese pregnant women.
Methods: This double-blind randomized controlled trial recruited pregnant women with a body mass index of 30.0-39.9kg/m2. Women were randomized to either a daily probiotic (Lactobacillus-salivarius UCC118) or placebo capsule from 24 to 28 week's gestation. The primary outcome was a reduction in fasting glucose from pre to post-intervention and secondary outcomes were incidence of gestational diabetes and neonatal anthropometry. A sample size of 100 was required to detect a reduction in fasting glucose of 0.4 mmol/l.
Results: Of 138 participants, twenty-eight were excluded from analyses due to antibiotic usage and poor capsule compliance, leaving 110 women for final analysis. BMI was the only factor that differed between the intervention groups at baseline (32.9±2.6 probiotic vs 34.0±2.7kg/m2 placebo, p=0.044). Adjusting for BMI, no difference was noted in fasting glucose from pre- to post-intervention (-0.07±0.41 probiotic vs -0.11±0.27 mmol/l placebo, p=0.295). There was also no difference in birth weight centile, incidence of gestational diabetes or other adverse pregnancy outcomes between the groups.
Conclusion: While previous studies of probiotics in healthy pregnant women showed some beneficial glycaemic effect, this randomized trial demonstrated no impact on fasting glucose or on obstetric outcomes in obese pregnancy.

I-25 Use of potassium iodide supplements improve antioxidant and anti-obesity properties of human milk

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Background and aims: Iodine is an essential micronutrient involved in fetal and infant neurodevelopment. In order to guarantee an adequate iodine supply during pregnancy and breastfeeding, the use of potassium iodide (KI) supplements is recommended. However, little is known about the relationship between KI supplementation in mothers and the properties of human milk.

Objective: To evaluate the effect of maternal KI supplementation on the composition of human milk, particularly different markers of oxidative stress, lipid peroxidation and obesity-related hormones present in breast milk.

Methods: 67 pregnant women, who received KI 300 µg/day from the first trimester of gestation to lactation period, were compared with 21 pregnant women (control group) who never received iodine supplements nor iodized salt. Breast milk samples were collected between 0-1 days after delivery.

Leptin, ghrelin, adiponectin, obestatin, glutathione peroxidase (GSH-Px) activity, superoxide dismutase (SOD)activity, catalase activity and thiobarbituric acid reactive substances (TBARS, an indicator of lipid peroxidation) were measured in the aqueous phase of breast milk.

Results: The iodine in breast milk correlated significantly with the activity of SOD (r=-0.459, p< 0.0001), catalase (r=-0.279, p=0.018) and GSH-Px (r=-0.302, p=0.011) , and with adiponectin levels (r=-0.505, p< 0.0001). The association between adiponectin and iodine remained significant (p=0.038) (R2 =0.430) after adjusting for SOD, catalase and GSH-Px activity and the body weight of the newborns.

Conclusion: Iodine may be a factor directly involved in the regulation of oxidative stress and adiponectin levels in human milk.

I-26 The association between maternal dietary antioxidant intake during pregnancy and neonatal anthropometry

EARLYNUTRITIONMEMBER

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Background: Maternal oxidative stress in pregnancy is associated with foetal growth. Maternal obesity increases oxidative stress and antioxidant supplementation has been found to reduce birth adiposity in rats. In humans, there has been some investigation into the association of serum antioxidant levels and neonatal size and adiposity but the effect of dietary antioxidant intake remains incompletely understood.

Aim: To examine the association of maternal dietary antioxidant intake with neonatal anthropometry.

Methods: This was a cohort analysis of 554 infants from the ROLO study. Abnormal intrauterine growth was an exclusion criterion. 3 day food diaries from each trimester were collected and maternal micronutrient supplementation recorded. Neonatal weight, length, arm, abdominal, chest and thigh circumference as well as biceps, triceps and subscapular skinfold thickness was measured at birth. Waist:hip circumference ratio and other ratios indicative of neonatal adiposity were calculated.

Results: Birth weight was negatively associated with trimester 2 vitamin E intake R2adj18.7% (F= 16.07, p=0.000). Abdominal circumference was negatively associated with trimester 1 selenium and trimester 3 vitamin E intake and positively associated with trimester 3 retinol intake R2adj5.0% (F= 2.04, p=0.038). Arm circumference was negatively associated with trimester 3 selenium intake R2adj4.2% (F= 2.12, p=0.044). Waist:hip circumference ratio was negatively associated with trimester 1 vitamin E intake R2adj6.7% (F=2.57, p=0.011).

Conclusion: Increased dietary antioxidant intake was associated with reduced birthweight and adiposity in a cohort at risk of macrosomia indicating the need for further research to determine whether this may be a possible area for dietary intervention.

I-27 The problem of non-participation: Who declined to participate in "Fit for Delivery", a randomized, controlled trial of a lifestyle intervention in pregnancy?

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Background: Fit for Delivery (FFD) is a randomized, controlled trial of a lifestyle intervention designed to limit gestational weight gain and increase physical activity in pregnancy. An investigation of reasons for non-participation was included in the design of the study.

Methods: Nulliparous women residing in southern Norway were invited to participate in FFD if they had a singleton pregnancy at ≤20 weeks gestation, age ≥18 years and body mass index (BMI) of ≥19. Women who declined participation were asked to complete an anonymous questionnaire with 7 questions. They were asked reason for non-participation (8 choices), age, height, pre-pregnancy weight, smoking status, educational level and frequency of physical activity. Study participants (n=606) completed a more comprehensive questionnaire before randomization. Responses were compared using independent-samples t-test and chi-square test for continuous and categorical data, respectively.

Results: Non-participants who completed the non-response questionnaire (n=60) most often cited satisfaction with their own nutrition and fitness plan (50%) and being too busy to exercise several days a week (43%). Compared with participants, non-participants were younger (mean difference 1.48 years, CI 0.51-2.65 (p=0.013)), more often smokers (12.5% vs. 4%, p=0.014), and fewer had ≥4 years of higher education (9.4% vs. 35.6%, p< 0.001). There were no significant differences between groups in weight, height, BMI or physical activity level.

Conclusion: There is a statistically significant difference in age, smoking and educational status between FFD participants and non-participants. BMI and activity level do not differ between groups. These finding may help us in developing future interventions and trials.

I-28 Infants fed formula with 2.3g of quality-improved protein per 100kcal showed the same growth as breast-fed infants

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High protein content of infant formula was reported to result in higher BMI of infants at 6 months of age, which might cause later obesity. We performed a large-scale survey on infants until 6 months of age to assess the growth of infants fed our commercial formula with

a protein content of 2.3 g/100kcal, protein and amino acid composition of which are improved. The growth and nutritional intake of breast-fed (12,418) and Meiji formula-fed (1,472) infants were researched by parental interview in Japan. Protein content (2.3 g/100kcal) of the formula is within the range (mean ± SD) of breastmilk protein content we measured. The amounts of each essential amino acid, alpha-lactalbumin, beta-lactoglobulin and large molecule protein in the formula are modified, in terms of protein quality, based on those of breastmilk we analyzed. Growth of the formula-fed infants was well-matched to that of breast-fed infants during the first 6 months. Daily protein intake of the formula-fed infants was lower in proportion to the decreased amount of protein content per energy, compared with infants fed our previous formula with a protein conent of 2.4 g/100kcal. In conclusion, infants fed our commercial formula with a protein content of 2.3 g/100kcal grew comparably to breast-fed infants. Protein content of the formula can be further reduced with protein quality improvement in various points.

I-29 Transplacental transfer of auto-antibodies to the fetus in pregnant women with type I diabetes and polyglandular autoimmune syndrome

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Background: Auto-antibodies against additional autoimmune diseases can be detected in 50% of patients with type I diabetes. So far only placental transfer of maternal antithyroid antibodies is known and can cause neonatal M. Basedow. In this study we investigated the transplacental transfer of autoantibodies of type I diabetes and associated autoimmune diseases.

Methods: In a prospective study we screened 22 nonselected patients with type 1 diabetes for their autoantibody status. In the case of positive antibody titers we than determined the corresponding antibody titer in the umbilical cord blood at time of delivery and in venous blood of the child during the first year of life.

Results: 86% of the screened patients had antibodies associated with type 1 diabetes, 50% had antithyroid antibodies, 14% anti-PCA antibodies and 4,5% had antibodies associated with celiac sprue. Placental transfer of maternal autoantibodies could be detected in 100% in cases of diabetes type 1 antibodies, in 62% in antithyroid antibodies and in 100% in cases positive for anti-PCA. All antibody titer were decreasing during the first year of life, but were still present at the age of one year.

Conclusion: We could proof that autoantibodies associated with maternal autoimmune disease are transferred to the fetus. Titers detected in the children correspond to the concentration found in the mother. The antibodies persist during the first year of life. The consequences for future health and disease have to be elucidated and we are currently continuing to monitor the children of this study.

I-30 Effects of testosterone propionate administration at puberty on serum insulin and testosterone levels in male offspring of hyperglycemic rats

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The effects of maternal hyperglycemia and 10 days of testosterone propionate administration at puberty on blood glucose and insulin level were investigated in male offspring. The male offspring of 100 female Wistar albino rats were used. A single intraperitoneal injection of alloxan (90mg/kg body weight) was used to achieve maternal hyperglycemia at different days of gestation (GD1, GD8 and GD15). The animals were subsequently given 10% glucose daily. Blood glucose, serum insulin and testosterone levels were assessed in the male pups. There was a significant increase in the fasting blood glucose level after testosterone (T) administration which was not accompanied by a significant difference in the mean serum fasting insulin level. The mean serum level of testosterone was significantly lower ($p < 0.01$) in all the groups (both testosterone treated and non-treated groups) except in GD15-21+T. Histological sections of the pancreas from experimental groups not treated with testosterone showed necrosis and infiltration by white blood cells which was not observed in the testosterone treated groups. It is deduced from this study that maternal hyperglycemia caused alterations of the endocrine pancreas in the male fetus, and a reduction of Testosterone level and that testosterone propionate administration at puberty may ameliorate some of these effects.

I-32 Dietary patterns and neurodevelopment in Greek preschool children

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Background: Several studies have investigated the role of diet in infancy with nutritional inadequacy at early ages being related to multiple neurological deficiencies. However, only few have examined the possible effect of a poor diet on neurological development in childhood. The aim of the study was to examine whether dietary patterns may affect neurodevelopment in children.

Methods: The present analysis included 803 preschool children from the Rhea mother-child cohort in Crete, Greece. The dietary assessment was conducted using a validated food frequency questionnaire and dietary patterns were identified using principal component analysis. McCarthy Scales of Children's Abilities (MSCA) were used to evaluate neurodevelopment at 4 years of age. Multivariable linear regression models were used to investigate the associations of dietary patterns with the MSCA scales.

Results: A 10g per day increase of fish intake resulted to a 1.05 (95% CI: 0.07, 2.02) increase in verbal, 1.11(95% CI: 0.09, 2.12) increase in quantitave and 1.06 (95% CI: 0.09, 2.02) increase in general cognitive scales after adjusting for confounders.

High adherence to Mediterranean dietary pattern, characterized by fruits, vegetables, fish and olive oil was associated with higher scores on almost all neurodevelopmental outcomes. However, after adjusting for potential confounders associations were attenuated and were no more statistically significant.

Conclusions: Results from this analysis indicate the possible beneficial effect of fish intake in early childhood on cognitive and language development of preschool children.

I-33 Birth weight, current anthropometric markers and high sensitivity C-reactive protein in Brazilian children

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Background: Studies have shown associations of low birth weight with increased adult concentrations of hs-CRP.

Objective: This study assessed the relationship between birth weight, anthropometric and metabolic parameters during childhood and hs-CRP.

Methods: 612 Brazilian children aged 5-13 years were included. Children's nutritional status was assessed by body mass index (BMI) and waist circumference (WC). Birth weight was categorized as small for gestational age (SGA), appropriate for gestational age (AGA) and large for gestational age (LGA). hs-CRP was measured by particle-enhanced immunonephelometry. Statistical analysis included Pearson, Spearman and partial correlations.

Results: Regarding birth weight, 2.1 (%) children were SGA, 79.6% AGA and 18.2% LGA. Medians for BMI, height and WC were significantly higher for LGA children compared to other birth weight categories ($p < 0.001$). LGA children showed higher hs-CRP levels than SGA children ($p=0.01$). There was a direct and significant correlation between hs-CRP and current BMI $r=0.42$; $p < 0.001$). There were no significant associations between hs-CRP and birth weight, HOMA, cholesterol and fractions, triglycerides and glucose.

Conclusions: Higher weights at birth and during childhood are associated with higher hsCRP levels. The association between low birth weight and chronic low-grade inflammation described in adults was not observed, but it is possible that this association takes a longer period to manifest. This may have implications for prevention, since interventions during childhood may prevent the progress of inflammatory processes later in life.

I-34 Physical Activity in Pregnancy - Results of the German Pilot Project: „9+12 Jointly Healthy in Pregnancy and Baby's First Year"

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According to the concept of metabolic programming physical activity and a balanced diet are relevant determinants to prevent obesity. The study examines mother's activity behavior in pregnancy at four stages (S1-S4). Therefore data from attending gynecologists are used. We analyze women's physical activity behavior during pregnancy with regard to the development of everyday life mobility and on sports (n=363). Additionally physical constraints caused by pregnancy are considered.

First results show that the majority of participants (57%) indicate no constraints in the beginning of pregnancy whereas only 15 % indicate strong constraints. At the end of pregnancy 28% report no limitations while 29% have strong constraints. Generally, two third of the sample show high rates of everyday life mobility (S1-3). For S4 a decrease is observable. Sports activity is generally low. Only 6% (S1) to 3% (S4) do regular sports and more than 76% do never or max once a week sports. The degree of physical limitations is decisive for the frequency of physical activity, especially sports. 80% (S1) to 91% (S4) of the participants with high constraints practice sports very seldom. The analysis will continue with a multivariate analysis on further determinants on physical determinants.

In conclusion, first results emphasize the need for further actions to improve physical activity especially sports during pregnancy. Therefore medical advisory service should inform how to handle physical constraints and clear up on the relevance for well-being and obesity prevention. As a sustainable strategy to prevent obesity, that issue should be also legally consolidated.

I-35 Preventing adverse health-related perinatal programming effects through social support

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Background: Both socio-economic status (SES) and social environment have major influences on health-related perinatal programming. Using existing access via social assistance programs for implementing specific interventions could be an option to minimize malprogramming and reduce lifelong health inequalities. Activities of "Early Aid" (EA) projects in Germany offer free-of-charge intensive pre- and postnatal care via family midwives (FM) for families with an increased need for psycho-social support. The aim of this study was to investigate the effect of an EA-project regarding psycho-social parameters.

Design: Data were collected by the service-delivering FM regarding the magnitude of various psycho-social problems (e.g. stress, lack of graduation) of the intervention participants. Overall, data from 295 families residing in Hessen (Germany) were analyzed. The extent of the individual problems at program entry and termination were documented and transformed into a score. Changes in score values were examined in total and stratified by migration, partnership status and SES.

Results: At program entry significantly higher score values were observed in single-parents ($p=0.004$) and those with low SES ($p < 0.001$). After the intervention the overall problem-score decreased significantly in the entire group ($p < 0.001$). After stratification single-parent families had significantly less improvement than couples ($p=0.015$), while neither migration nor SES were related to score improvement.

Conclusions: EA-projects could be important components in the prevention of malprogramming and health inequalities. Persons with assumed lower social support (as indicated by single-parent status) may need specific support to achieve improvements. Therefore, reliable and beneficial social support should be focused by FM.

I-36 A prospective observational clinical study: "The role of human milk in development of breast fed child's intestinal microbiota" -study design and selected results

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Objectives: A design, objectives and basic results of the prospective observational clinical study on Slovenian pregnant and lactating women and their newborns, aimed to establish a link among mother's diet, human milk long chain polyunsaturated fatty acids (LCPUFA) composition and microbiota, and their influence on child's gut microbiota development and health in the first year, are presented.
Methods: Pregnant women were recruited in central, Pannonial and Mediterranean regions. All participants (n=294) were involved in long-term dietary habits assessment by Food frequency questionnaire (FFQ), while 63 % participated also in in the assessment of dietary habits by 4-days weighed protocol (4DP), medical examinations during the pregnancy and the first year post-partum (anthropometric measurements, health status of mothers/infants, development of infants, and bone mineral density measurements of mothers/infants) and biological samples collection. Samples were subjected to determination of vitamin D content in serum, fatty acid composition in plasma, fatty acid composition and microbial composition of human milk, and of infants` faecal microbiota.
Results: FFQ data were obtained from 294 pregnant women recruited from December 2010 to October 2012, 4DP data from 185 and biological samples from172 mother/child pairs. The analyses of plasma (vitamin D, 133 samples; fatty acids, 154 samples) have been completed. Microbiota of colostrum (118), human milk (285), meconium (96) and newborns' faeces (410) is being analysed by conventional and molecular methods, including new generation sequencing (NGS).
Conclusion: The study will provide valuable data on the nutrition of Slovenian pregnant and lactating women, and contribute new knowledge on the mechanisms of infant's intestinal colonisation.

I-37 Public awareness of fayoum population about their body measurements

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The prevalence of obesity is increasing worldwide. There was general agreement that BMI surveillance was an epidemiologic tool for the assessment of obesity in different populations. The aim of this study is to screen community awareness about body measurement, and to examine actual body weight with self-perception of body image.
Methods: This study was a community-based survey conducted in Fayoum Governorate. We used multistage stratified random sampling to select the study household with a number of participants (582). We developed a self-administrated structured questionnaire. Anthropometric assessment weight, height and waist circumference were measured and BMI was calculated.
Results: Our results showed that the prevalence of obesity was 88.7% with a more in female than male. More than half of the participants knew their weight and height Overall, 40.6% of women and 38.8% of men misclassified their own weight status by BMI. There was a statistical significant difference between knowing weight and height, and their accurate results (P=0.000).
Conclusion: Our results showed that the majority of the Fayoum population was obese. Implementation of health promotion and health education in the community should use effective nutrition education in the mass-media to raise awareness of appropriate body weight and healthy lifestyle.

I-38 Relevance of ultrasound parameters during treatment of twin pregnancies with Diabetes

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Background: According to the new guidelines for treatment of diabetes in pregnancy target values of blood sugar levels are defined depending on fetal growth, especially the growth of the abdominal circumference. In twin pregnancies abdominal circumference of the two fetuses often tend to deviate during the course of pregnancy. The guidelines so far do not state on which fetus should be leading the therapeutic regime in such cases of diabetic twin pregnancies.
Method: Case reports of four diabetic twin pregnancies with growth deviation of the fetuses and the influence of the amternal blood sugar level on the fetal growth curves in these pregnancies.
Results: In all pregnancies maternal targeted blood sugar levels had to be elevated due to deceleration in growth of one twin. In all cases elevation of the daily medium blood sugar level (> 6,0 < 6,5 mmol/l) reversed the growth deceleration in the affected twin without being followed by acceleration in growth of the second twin.
Conclusion: For the management of twin pregnancies the growth of the smaller twin should be guiding therapeutic decisions. Furthermore our data suppose that diabetic twin pregnancies might benefit from higher target blood sugar levels.

I-39 Composition of infant formula and the impact of home reconstitution on nutrient density

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Aim: of the present exploratory investigation was to evaluate the impact of home reconstitution on nutrient density based on data that was collected in a double-blind RCT studying the effect of three hydrolysed formulas on growth (analysis ongoing). In order to evaluate the home reconstitution procedure, bottles were prepared by the mother at their infant's age of 4 and 12 wks and collected for chemically analysis of nitrogen (nitrogen analyzer EP Analyzer EP 428; Leco France) and fat ("Soxhhlet" Soxtec Aventi 2055; Foss).
Results: In all 333 bottles were analyzed. In 6 bottled, the results of the fat and the nitrogen contents were discordant, and the results were excluded of the final analysis. The protein contents (g/100ml, mean±SD and ranges) were 1.24±0.10 , 1.01-1.48, for F1 ; 1.39±0.11 , 1.09-1.64, for F2 ; and 1,58±0.13, 1.26-1.83, for F3 ; slightly higher than the labelled values, 1.19, 1.32 and 1.50g/100mL respectively. There is a large overlapping of the protein content between the formulas.
Formula density estimated from the fat analysis was 1.005±0.066, (0.849 to 1.151) and was similar in the 3 formulas. Formula density

at 12wks was significantly correlated to the density at 4 wks (r^2= 0.22, p< 0.0001) suggesting that the reconstitution procedure by the mothers were relatively reproducible.
In conclusion, our study suggests that the reconstitution procedure at home significantly influences nutrient density of the studied formulas and needs to be taken into account in the interpretation of the results of nutritional studies performed in healthy term infants.

I-40 Nutrient intake status in healthy toddlers - A comparison of intake data from four countries in different stages of socioeconomic development

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Accumulating research through the past few decades continues to highlight the role nutrition plays during early childhood and its preventative effect on factors relevant to health later in life including cardiovascular health, allergies, bone health, and the development of obesity. Inadequate (micro)nutrient intakes are not restricted to developing countries, but have been reported also for transitional nations, e.g. the former Soviet Union, as well as for industrialized countries such as Germany. However, up-to-date comparative research on this topic from different regions of the world is still limited.
We conducted a literature review to examine the (micro)nutrient intake status in healthy toddlers from the most populous countries from four geographical regions representing different stages of socioeconomic development: Germany, Russia, USA, Brazil. We searched for national representative surveys conducted from 2000 to 2013 and published either in English or in the national language of the respective country. To identify eligible studies, we searched for published data (e.g., in Pubmed) as well as for unpublished grey literature. Unpublished data were also requested from authors directly. The outcome of interest was the intake status of essential (micro)nutrients such as vitamins A, D, E, folate, calcium, iron, zinc, and polyunsaturated fatty acids reported as population mean or median.
The findings of this on-going study might support pediatricians, nutritionists, public health researchers and policy makers to implement country-specific strategies to prevent micronutrient deficiencies during the first years of life.

I-41 Consumption of fruits and vegetables among Romanian pregnant women

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The healthy nutrition guidelines proposed by international research institutes and World Health Organization recommend a daily intake of fruits and vegetables of a minimum 400 g, representing 5 servings/day (each serving having around 80 g). The present study aims to identify the knowledge, attitudes and behavior related to consumption of fruits and vegetables among Romanian pregnant women. A cross-sectional study was performed in September-November 2011 by means of anonymous questionnaires among 160 pregnant women aged 20-38 in the second and third semester of pregnancy from Cluj-Napoca, Romania. The results show that half of the pregnant women included in the study declared the consumption of fruits and vegetables every day in the last week, but only 11.2% have eaten 5 portions of fruits and vegetables daily. One third of the study sample have discussed with a health care professional about the importance of consuming fruits and vegetables during pregnancy, but only 16.8% have known which are the recommendations regarding the number of servings of fruits and vegetables which should be consumed daily. Around 40% of the pregnant women declared their intention to consume more fruits and vegetables in the next month. The results underline the need for educational activities targeting Romanian pregnant woman regarding the importance of eating minimum 5 portions of fruits and vegetables daily, as an important component of a healthy diet.

I-42 Relationship between alpha-tocopherol concentrations with lipid profile and insulin resistance in adolescents with acquired immunodeficiency syndrome

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Objective: To describe the plasmatic concentrations of alpha-tocopherol in adolescents with acquired immunodeficiency syndrome (AIDS) and to correlate alpha-tocopherol concentrations with lipid profile and insulin resistance.
Methods: In cross-sectional and controlled study 38 AIDS patients receiving antiretroviral therapy (median length of treatment 28.4 months) were evaluated. The control group was of 30 uninfected healthy adolescents matched for age and gender. Clinical and laboratory assessments were performed to determine nutritional status (z-score of body mass index and height/age), plasmatic concentrations of alpha-tocopherol, lipid profile (HDL-c, LDL-c, triglycerides, non-hdl-cholesterol), glycemia and insulin (to calculate homeostasis model assessment for insulin resistance - HOMA, cutoff >3). Statistical analysis: Mann-Whitney and Chi-square tests.
Results: The median of age was 13.5 years and HIV stage was B2 (42.1%) was the more often. In the AIDS group the median of alpha-tocopherol/triglycerides concentration was lower (7.0 vs 19.3 ug/mg; p< 0,001) and inadequate values for LDL-c (20.0% vs 0.0% vs 6.7%, p=0.024) were more often than in the control group. There isn´t association between alpha-tocopherol concentrations with lipid profile and HOMA-IR.
Conclusions: The association between low alpha-tocopherol concentrations and high frequency of LDL-c may increase the risk for chronic diseases in AIDS adolescents.

I-43 Long-term follow up of inadequate feeding in infancy

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Introduction: The interest in studying the follow up results of feeding with non-adapted dairy products is associated with the extensive research based on the theory of metabolic programming according to which inadequate nutrition at the early stages of infant develop-

ment is a cause of various diseases in adults.
Objective: To study the long-term follow up results of inadequate feeding in infancy
Materials and methods: 109 children on different types of feeding in infancy were investigated. We studied the characteristics of feeding, the basic food, analysis of their physical development data, as well as the protein, fat and carbohydrate metabolism and BP parameters.
Results: In the retrospective analysis of pre-, intra-and post-natal development we revealed the relative risk factors for starting bottle feeding with non-adapted dairy products. The analysis of the daily diets of schoolchildren showed excessive carbohydrate intake, the disturbance of energy balance, conforming to the stereotype of unhealthy food. In bottlefed children there was a tendency towards growth stimulation at all age intervals, but it was more displayed in infants and young children. Obviously, it can be explained by excessive protein intake by children of the group.The bottlefed children had not only the higher values of BP within the norm, but also presented with high normal BP and arterial hypertension, as well as with changes in fat and carbohydrate metabolism.
Conclusion: Inadequate feeding is the risk factor for physical development impairment and the change in nutritious status and it can lead to the metabolic syndrome development.

I-44 Screening of MC4R gene as early prevention for obesity

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Obesity is defined as having an excessive amount of body fat. It did not only occurs in adult but also in children. Obese children are more dangerous because they are more likely to develop chronic disease like cardiovascular disease and diabetes at a younger age. In 2011, prevalence of obesity in children under the age of five, is estimated to be over 40 million. The etiology are prenatal and postnatal nutrition, lifestyle, unhealthy diet and genetics. Mutation of MC4R gene is associated with the risk for being obese genetically. Someone who suffered from MC4R mutation will have a high risk for having an obese children. This will increase incidence of obesity. So, genetic testing of MC4R gene will be one of the way for early prevention for obesity. This abstract reviews publications on MC4R gene, MC4R genetic testing and obesity which have appeared in every research-related literature found online. Results were limited to
(1) English-language articles,
(2) publication year 2008 or later, and
(3) publication types including clinical trials, controlled clinical trials, meta-analysis, randomized controlled trial, or review.
Mutation of MC4R gene, either heterozygous or homozygous genotype, will produce an abnormal eating behavior. Mutation carriers (heterozygous genotype) had severe obesity, increased lean mass, increased linear growth, hyperphagia, and severe hyperinsulinemia. Homozygotes genotypes result in more severe clinical manifestation. Mutation of MC4R gene is associated with increased risk of obesity and become the leading cause for abnormal eating behavior. Early screening of this gene using PCR can be used as prevention for obesity.

I-45 Selective nocturnal insulin resistance in gestational diabetes - a case report

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Background: In cases with glucose intolerance during pregnancy the impact of moderate isolated elevated fasting glucose levels is not discussed so far.
Methods: We describe a case report of isolated moderately elevated fasting glucose levels and associated acceleration in fetal growth, where the acceleration of abdominal growth could be reversed by treatment with long acting insulin at night.
Results: We report about a 28 year old women presenting at 31 weeks of gestation because of acceleration in growth and amount of amniotic fluid. Routine testing for gestational diabetes was done at 24 weeks of gestation and revealed normal at that time point. No history of diabetes during the first pregnancy. Family history with diabtes type II and adipositas. The repeated 75 oral glucose tolerance test revealed pathologic (fasting: 5,3 mmol/l, 1h: 7,7 mmol/l, 2h: 6,7 mmol/l). The daily glucose levels than showed elevated fasting glucose levels and we started treatment with long acting insulin at night in raising quantity, until fasting glucose levels were < 5,0 mmol/l. Abdominal growth could be reversed to normal and a healthy girl was born at 40 weeks of gestation.
Conclusion: Isolated even if moderate elevation of fasting glucose levels might be so far under considered during treatment of gestational diabetes in pregnancy

I-46 Survey of effect sheep's milk on grow and health of infants with sensitivity to protein of cow's milk

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Background and aims: Sensitivity to protein of cow's milk is increasing among infants in developing countries such as Iran. Some problems of sensitivity to protein of cow's milk include skin signs and gastrointestinal problems. Therefore, the article focuses on replacement other milk products instead of cow's milks in diet of nursing mothers with infants suffering to sensitivity to protein of cow's milk.
Methods: Participants of study were 10 nursing mothers and their infants who were referred to a nutrition and dietetics center in Tehran/Iran. The collection data were focused interview and consultant dietitian with nursing mothers. In continues, the researchers conferred with the neonatal specialists about the finding of focused interview with nursing mothers.
Results: The findings of study show that 7 infants of participants have sensitivity to protein of cow's milk. However, dried milk with protein hydrolyzed is often recommended for the infants by the neonatal specialist; but the milk has bitter taste and the infants don't like and eat it; therefore their growth will be impaired.
Conclusion: According to the results of study, the researchers suggest two solutions. The first solution is the replacement bufflehead's milk instead of cow's milk in diet of nursing mothers. The experimental observations show that the number of infants with sensitivity to protein of cow's milk can tolerate protein of bufflehead's milk. The second solution is the replacement sheep's milk instead of cow's milk in diet of nursing mothers that fortunately, the majority of infants can tolerate the protein of milk.

II - Epidemiology

II-1 Maternal inflammation during pregnancy and mid-childhood adiposity

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Background: Maternal pre-pregnancy obesity is associated with an increased risk of obesity in offspring, possibly via an increased pro-inflammatory state during pregnancy.

Methods: In Project Viva, among 521 mother-child pairs, we examined associations of maternal 2nd trimester plasma levels of CRP, TNF-α, IL-6, and IL-10, measured by bead-based multiplexing technology, with mid-childhood (age 7-10 y) BMI-z, waist circumference (WC), and DXA fat mass index (FMI), trunk fat mass index (trunkFMI), and fat-free mass index (FFMI). We performed linear regression models adjusted for gestational age at blood draw, maternal age, pre-pregnancy BMI, education, parity, smoking, race/ethnicity, and child age and sex.

Results: Median (IQR) maternal cytokine levels (ng/ml) were CRP-1.2 (0.6, 21), TNF-α-28.0 (4, 60), IL-6-24.5 (11, 43), and IL-10-48.5 (26, 90), respectively. Mean (SD) mid-childhood BMI-z, WC, FMI, trunkFMI and FFMI were 0.39 (0.99), 59.7 cm (7.7), 4.4 kg/m2 (1.9), 1.5 kg/m2 (0.8), and 13.0 kg/m2 (1.4), respectively. Compared with the lowest quartile of maternal CRP, the highest quartile was associated with higher mid-childhood BMI-z (0.2 [95% CI: -0.1, 0.4]), WC (1.5 cm [-0.3, 3.3]), FMI (0.7 kg/m2 [0.1, 1.2]) and trunkFMI (0.3 kg/m2[-0.1, 0.5]), but not with FFMI (0.0 kg/m2 [-0.3, 0.4]) We did not find associations of maternal TNF-α, IL-6, or IL-10 with mid-childhood adiposity measures.

Conclusions: Higher 2nd trimester maternal level of CRP, a non-specific marker of inflammation produced by the liver, was associated with higher mid-childhood overall adiposity and possibly with central adiposity.

II-2 Maternal smoking during pregnancy and development of higher body mass index and blood pressure during childhood

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Objective: Obesity, and in some studies blood pressure, are higher among offspring of women who smoked during pregnancy, but at what ages these phenomena emerge is less clear. We examined associations of maternal prenatal smoking with child BMI and systolic blood pressure (SBP) from birth to mid-childhood (7-10 y).

Methods: Among 1755 mother-child pairs in Project Viva, we categorized mothers into never, former, or pregnancy smokers. Using repeated height/weight and SBP measures, we ran mixed models to estimate associations of maternal smoking with longitudinal BMI z-score and SBP from birth to mid-childhood, adjusted for maternal and child socio-demographics, pre-pregnancy and paternal BMI, gestational weight gain, environmental smoke, and breastfeeding duration.

Results: 68% mothers never smoked, 20% were former smokers, and 12% smoked during pregnancy. In mid-childhood, mean (SD) BMI z-score and SBP were 0.39 (1.0) and 94.6 mmHg (8.7). BMI z-score among offspring of mothers who smoked during pregnancy was not higher at birth or in infancy, but was 0.22 higher (95% CI 0.02-0.42) than never smokers in early and mid-childhood. Offspring SBP of both former smokers (1.5 mmHg; 0.5-2.5) and pregnancy smokers (2.2; 0.7-3.6) was higher than never smokers from birth onwards. After additional adjustment for BMI, SBP estimate for former smokers was not changed; for pregnancy smokers it was attenuated to 1.8 mmHg (0.4-3.2).

Conclusion: Pregnancy smokers had children with higher BMI-z score starting in early childhood. SBP was higher among offspring of both former and pregnancy smokers, from birth onwards and independent of child BMI.

☆ ***New Investigator Award***

II-3 Infant dietary patterns and bone mass in childhood: The Generation R Study

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Background and objectives: Nutrition in early life may affect peak bone mass attainment and future fracture risk. Previous studies on childhood nutrition and bone health have mainly focused on individual nutrients. Evaluating dietary patterns may better account for the cumulative effects of multiple nutrients. We investigated the associations between dietary patterns in infancy and childhood bone health in 2850 children participating in the Generation R Study.

Methods: Dietary information was obtained from a food frequency questionnaire at 14 months. Using principal component analysis, three dietary patterns were extracted. At the age of 6 years, a total-body DXA scan was performed. Bone mineral density (BMD), bone mineral content (BMC), area-adjusted BMC (aBMC), and bone area were analyzed.

Results: A higher adherence score to a "Dairy and whole grains" pattern was positively associated with BMD and aBMC, and inversely associated with bone area (P-values< 0.01). Additionally, children in the highest quartile of the "Dairy and whole grains" pattern had a higher BMD (difference 4.92 mg/cm2, 95%CI 1.34-8.51) and aBMC (difference 6.55g, 95%CI 2.89-10.21), and a smaller bone area, as compared to children in the lowest quartile. Other dietary patterns like "Potatoes, rice and vegetables", and "Refined grains and confectionary" were not consistently associated with bone outcomes.

Conclusions: In this prospective cohort study, a "Dairy and whole grains" pattern in infancy was associated with higher BMD later in

childhood. Further research is needed to explore the underlying mechanisms, and to investigate whether the observed differences have consequences for bone health in later life.

II-4 Protein intake in early childhood and kidney function at school age: The Generation R Study

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Background and objectives: Studies in children with renal disease suggest adverse effects of high protein intake on kidney function. Whether protein intake is related to kidney outcomes in healthy children is unclear. Therefore we examined the associations of total, animal and vegetable protein intake in early childhood with kidney volume and function at school age, in 2,908 children participating in a prospective population-based study.
Methods: Protein intake was assessed with a food frequency questionnaire at the age of 14 months and adjusted for energy intake. Kidney volume, serum creatinine and cystatin C levels, and urinary albumin and creatinine levels were measured at the age of 6 years. Glomerular filtration rate was estimated using serum creatinine levels and microalbuminuria was defined based on urine albumin and creatinine levels using clinical cut-offs.
Results: Animal protein intake was not associated with any of the outcomes. Higher vegetable protein intake was associated with lower serum creatinine and cystatin C levels (difference in cystacin C levels for highest vs. lowest quartile of vegetable protein intake: -0.20 (95%CI -0.39, -0.01) SD), and a higher glomerular filtration rate (difference: 0.19 (95%CI 0.02, 0.37) SD). Protein intake was not associated with kidney volume or the risk of microalbuminuria.
Conclusions: Our findings in healthy children suggest that vegetable, but not animal, protein intake in early childhood may be associated with kidney function in childhood. Further follow-up studies are needed to investigate whether protein intake in early life affects the risk of kidney diseases in later life.

II-5 Vitamin D measured in maternal serum and offspring cognitive outcomes at 20 years of age

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Background: There is evidence that vitamin D influences neuronal differentiation, endocrine functions, and fetal brain growth. Animal studies indicate alterations in the offspring brain as consequence of vitamin D-deficiency during pregnancy. In humans maternal vitamin D insufficiency has been linked with impaired child language development.
Aim: The aim of this study was to examine the association of maternal concentration of 25(OH)D with proxies of offspring neurodevelopmental outcomes.
Methods: Between 1988-89 pregnant women (n=965) were recruited for a prebirth cohort in Aarhus, Denmark. 25(OH)D was quantified in serum from week 30 of gestation by the LC-MS/MS method (n=850). Offspring were followed-up through national registries until age 20 years. We evaluated the association of maternal concentration of 25(OH)D with offspring neurodevelopmental outcomes, defined as: first admission diagnosis or prescription of medication for (1) ADHD; (2) depression; (3) scholastic achievement by mean grade at standardized written examinations in 9th grade (final exams of compulsory school in Denmark).
Results: Maternal concentration of 25(OH)D was higher compared to current levels (median (5-95%) 76.2 (23.0-152.1) nmol/l). During follow-up we identified 27 (3.1%) ADHD cases, 104 (11.9%) depression cases and the mean scholastic achievement was 6.7 (SD 2.3). Overall we found no association for maternal 25(OH)D with offspring behavioural and affective disorders or with scholastic achievement.
Conclusion: Our analyses based on biomarker measurement of 25(OH)D from a cohort of 850 pregnant women combined with 20 years of follow-up showed little support for an association between vitamin D status in pregnancy and clinically relevant offspring neurodevelopmental outcomes.

II-6 Maternal gestational weight gain in different trimesters and childhood cardio-metabolic outcomes. The Generation R Study

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Excessive gestational weight gain seems to be associated with offspring cardio-metabolic risk factors. We examined the associations of maternal trimester specific weight gain with childhood cardio-metabolic risk factors. In a population-based prospective cohort study from early pregnancy onwards among 5,908 mothers and their children, we obtained maternal prepregnancy weight and weight in each trimester of pregnancy. At the age of 6 years, we measured childhood body mass index, total body and abdominal fat distribution, blood pressure and blood levels of lipids, insulin and c-peptide. Independent from maternal prepregnancy weight and weight gain in other trimesters, higher first-trimester weight gain was associated with higher childhood body mass index, total fat mass, android/gynoid fat mass ratio, abdominal subcutaneous fat mass, systolic blood pressure, insulin and c-peptide (p-values< 0.05). Higher second-trimester weight gain was independently associated with higher childhood body mass index, total and abdominal subcutaneous fat mass levels and systolic blood pressure (p-values< 0.05). The associations for childhood cardio-metabolic outcomes attenuated after adjustment for childhood body mass index. Third-trimester weight gain was not associated with childhood outcomes. Higher first-trimester, but not second-

or third-trimester, weight gain was associated with increased risks of childhood overweight and clustering of cardio-metabolic risk factors (Odds Ratio (OR) 1.18 (95% Confidence Interval (CI): 1.07, 1.30) and OR 1.20 (95% CI: 1.06, 1.35) per standard deviation increase in first-trimester weight gain, respectively). In conclusion, higher weight gain in early pregnancy is associated with an adverse cardio-metabolic profile in offspring. This association is largely mediated by childhood adiposity.

II-7 Maternal seafood consumption and preterm delivery in a large Norwegian pregnancy cohort

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Preterm delivery is a major cause of perinatal morbidity and mortality. Maternal diet has been shown to influence the risk of preterm delivery. Seafood is an important source of nutrients but is also a source of environmental pollutants. The aim of this study was to examine associations between maternal intake of seafood and supplementary long-chain marine polyunsaturated fatty acids (n-3 LCPUFA) and preterm delivery. The study population comprised 60,761 women participating in the Norwegian Mother and Child Cohort study during 2002-2008. Maternal diet was assessed prospectively in mid-pregnancy using a validated food frequency questionnaire. Birth outcomes were obtained from the Norwegian Medical Birth Registry. Preterm delivery was defined as onset of delivery before gestational week 37. We estimated hazard ratios (HR) and 95% confidence interval (CI) using Cox regression models and adjusted for relevant confounding variables. Consumption of seafood corresponding to at least one serving per week (20-40 g/d) was associated with 20-30% risk reduction in comparison with no/seldom intake (< 5g/d); HR:0.75 (95%CI: 0.65, 0.88) for 1-2 servings/week (20-40g/d) and HR: 0.70 (95%CI: 0.59, 0.82) for 2-3 servings/week (40-60g/d). The risk reduction was mostly explained by the intake of lean fish. For oily fish only low intake was associated with lower risk. Intake of supplementary n-3 LCPUFA was not associated with preterm delivery. These findings support the current advice to include fish and seafood as part of a balanced diet during pregnancy.

II-8 Influence of genetic variants of the TAS2R38 bitter receptor gene on the intake of sweet tasting food, nutrient intake and body weight of European children

EARLYNUTRITIONMEMBER **Poster of Distinction**

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We aimed at studying whether genetic variants of the TAS2R38 bitter receptor gene influence energy intake from sweet tasting food, energy and macronutrient intake, and body weight in children.

Children (n=573) from five European countries were grouped into taster and non-taster by the first variant site rs713598. Three-day weighed dietary records were yearly obtained from the age of 12 until 72 months. Food items were grouped into sweet and not sweet tasting food. Mixed models were used to describe group differences in food and nutrient intake and body weight over time.

Intake of sweet tasting food increased from averaged 251 kcal/d at 12 months to 462 kcal/d at 72 months. Polish children had the highest caloric intake from sweet tasting food, while the intake in Italy was the lowest. Boys had a significant higher intake of sweet tasting food per day than girls (difference 17 kcal; 95% CI 2.2 - 31.6; p=0.028). The genetic taster status had no influence on the intake of total energy, macronutrients or sugar, or on body weight. However, between 12 and 72 months of age, tasters consumed an added 24 kcal per day (95% CI 4.4 - 43.9; p=0.017) from sweet tasting food than non-tasters. The influence of genetic taster status on intake of sweet tasting food tended to decrease over time.

Intake of sweet tasting food is influenced by multiple factors. Genetic taster status is linked to energy intake from sweet tasting foods. Gender and country influence the intake of sweet tasting food items.

II-9 Gestational weight gain in normal weight women is associated with offspring cardio-metabolic risk factors at 20 years of age

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Background: Limited knowledge exists on the long-term implications of maternal gestational weight gain (GWG) on offspring health, particularly among women of normal pre-pregnancy weight (body mass index (BMI): 18.5-24.9 kg/m2).

Objective: To examine whether high GWG in normal weight women is associated with adult offspring cardio-metabolic risk factors.

Methods: We used a cohort of 308 Danish women who gave birth in 1988-89 and whose offspring participated in a clinical examination at 20 years of age. Main outcome measures were offspring BMI, waist circumference, weight-regulating hormones, blood lipids, and glucose metabolism. Associations were assessed using multivariate linear and logistic regression models.

Results: A weak positive association was observed between GWG during the first 30 weeks and offspring anthropometry. Each 1-kg increase in maternal GWG was associated with 0.1-kg/m2 increase (95%CI: 0.01, 0.2) in offspring BMI and 10% (95%CI: 0.0%, 20%) increased odds of offspring overweight at the age of 20 years, with similar associations observed in both sexes. However, sex differences were observed for the association between maternal GWG and specific cardio-metabolic risk factors. Hence, per 1-kg increase in GWG, HOMA-IR increased 3.4% (CI; 0.8, 6.0%), insulin increased 3.7% (95%CI: 1.4%, 6.2%), and leptin increased 10.7% (95%CI: 5.7%, 15.9%) in male offspring. These associations were not observed in females, which may partly be explained by more frequent reports of

dieting and physical exercise at follow-up among female offspring.
Conclusion: In normal-weight women, high GWG may have modest long-term implications on offspring cardio-metabolic risk factors at adult age.

II-10 General and abdominal adiposity measures associated with C-reactive protein in school-age children

EARLYNUTRITIONMEMBER *Poster of Distinction*

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Background: High body mass index is associated with increased C-reactive protein levels in childhood and adulthood. Not much is known about the associations of more specific general and abdominal fat mass measures with C-reactive protein levels in childhood.
Methods and Results: We performed a population-based cohort study among 4,338 school-age children (median age 6.0 years (95% range 5.7-7.5 years)) to examine the associations of childhood body mass index, total body fat mass and android/gynoid fat mass ratio assessed by Dual-energy X-ray Absorptiometry and pre-peritoneal abdominal fat mass assessed by ultrasound with C-reactive protein levels. Increased C-reactive protein levels were defined as the upper 10% (>3.1 mg/l). Of all children, 82.3% had a normal weight and 17.7 % were overweight or obese. The odds of increased C-reactive protein were higher among overweight and obese children (OR: 1.85 (95% CI 1.43, 2.40) per SDS increase in total body fat mass). Compared to body mass index, total fat, android/gynoid fat ratio and pre-peritoneal fat were stronger correlated with C-reactive protein levels. In logistic regression models adjusted for age, sex, height and ethnicity, increased childhood adiposity measures were associated with higher odds of having an increased C-reactive protein, with the strongest effect for total body fat mass (OR: 1.43 (95% CI 1.28, 1.60) per SDS increase in total body fat mass).
Conclusion: Total and abdominal fat mass outcomes are associated with increased C-reactive protein levels in childhood. These findings suggest that body fat distribution is associated with a proinflammatory status in school-age children.

Poster

II-11 Prenatal famine and mortality between age 18-63 years from cancers, cardiovascular disease and other causes

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ome studies show an increase in mortality after prenatal exposure to famine. We examined this relation in more detail in 25,283 men born around the time of the Dutch famine of 1944-1945 in six affected cities in the Western Netherlands, 10,667 unexposed time controls born before or after the famine in the same cities and 9,087 unexposed place controls born in areas not affected by the famine. All men were identified from national examinations at age 18 for military service. We traced the men through national registration systems to establish vital status and cause of death at age 63. We used Cox proportional hazards models with competing risks to estimate hazard ratio's (HR) and 95% confidence intervals (CIs) for selected causes of death.
We found 1,938 deaths from cancers, 1,038 from heart diseases, and 2,032 from other causes. Prenatal famine in the three pregnancy trimesters combined was not associated with deaths from cancer (HR 1.01; 95% CI: 0.91 to 1.12), heart disease (HR 1.05; CI: 0.92 to 1.21) or other causes (HR 1.06; CI: 0.96 to 1.17). In subgroup analysis, we observed an increase in deaths from diabetes mellitus after prenatal famine (HR 1.40; CI: 1.07 to 1.84) but the number of these deaths was small (n=244)..
Although especially the diabetes findings are intriguing, more reliable estimates are needed for selected causes of death as the cohort ages. Over time, this study will then be able to address fundamental questions on the developmental origins of long-term health in national data.

II-12 Maternal fish consumption during pregnancy and BMI development among their children followed for 14 years; the PIAMA birth cohort study

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Background: There is evidence that n-3 fatty acid exposure in utero might influence early human adipose tissue development and risk of obesity later in life. Fish is an important dietary source of n-3 fatty acids. Few epidemiological studies have been conducted in this area.
Aim: To investigate the longitudinal association between maternal fish consumption during pregnancy and BMI development of their children followed for 14 years.
Methods: The study population consisted of 3963 Dutch children born in 1996-1997 who participated in the PIAMA birth cohort study. Data on maternal fish consumption during pregnancy and body weight and height at age 0.5, 1 till 8, 11 and 14 years were obtained by questionnaires. Generalized estimating equations (GEE) were used to investigate whether BMI development of the child, measured as BMI standard deviation scores (SDS), differs between groups with different maternal fish consumption during pregnancy. Multivariate models were adjusted for maternal and child lifestyle characteristics.
Results: Children's BMI development from birth up to age 14 years differed statistically significantly between groups of maternal fish consumption (p=0.03). Children of mothers who consumed fish once a week or more had a 0.1 to 0.2 SDS lower BMI than children of mothers who never consumed fish during pregnancy. Until 2 years of age differences in BMI were small, but differences became larger and statistically significant at later ages.
Conclusion: The results of this birth cohort study suggest that maternal fish consumption during pregnancy might be of importance for later BMI development of the child.

II-13 Can physical activity modify the programming effect of low birth weight on insulin resistance in adolescents?

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Objective: To examine whether physical activity influences the association between birth weight and insulin resistance in adolescents.
Methods: The study comprised adolescents who participated in two cross-sectional studies: the HELENA (Healthy Lifestyle in Europe by Nutrition in Adolescence) study (N=520, 14.6 years-old), and the Swedish part of the EYHS (European Youth Heart Study) (N=269, 15.6 years-old). Participants had valid data on birth weight (parental recall), body mass index (BMI), sexual maturation, maternal education, breast feeding, physical activity (accelerometry, counts/minute), fasting glucose and insulin. Insulin resistance was assessed by homeostasis model assessment (HOMA-IR). Maternal education level and breast feeding duration were reported by the mothers.
Results: There was a significant interaction of physical activity in the association between birth weight and HOMA-IR (Ln transformed) in both the HELENA study and the EYHS (P=0.05 and 0.03, respectively), after adjusting for sex, age, sexual maturation, BMI, maternal education level and breast feeding duration. Stratified analyses by physical activity levels (below/above median) showed a borderline inverse associations between birth weight and HOMA-IR in the low active group (standardized β= -0.094, P=0.09; and standardized β= -0.156, P=0.06; HELENA and EYHS, respectively) while no evidence of association was found in the high active group (standardized β= -0.031, P=0.62; and standardized β= 0.053, P=0.55; HELENA and EYHS, respectively).
Conclusions: Higher levels of physical activity may attenuate the adverse effects of low birth weight on insulin sensitivity in adolescents. More observational data, from larger and more powerful studies, are required to test these findings.

II-14 Maternal caffeine consumption during pregnancy and the risk of obesity in offspring: A prospective cohort study with 15 years of follow-up

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Objectives: The present study examines the impact of high maternal caffeine intake during pregnancy on the risk of childhood obesity in offspring.
Design: A prospective cohort study of pregnant women with 15 year follow-up of their offspring.
Setting: Kaiser Permanente member population in the San Francisco area.
Participants: Pregnant women and their offspring from the index pregnancy.
Exposure(s): Maternal caffeine intake during pregnancy.
Main Outcomes : Obesity measured by BMI >95th percentile against the CDC age- and gender-specific standard among the offspring of the index pregnancy ascertained from medical charts up to 15 years of age.
Results: After controlling for potential confounders, maternal daily caffeine intake ≥150 mg/d was associated with more than twice the risk of childhood obesity: odds ratio (OR) =2.1, 95% confidence interval (CI): 1.22-3.50, compared with no caffeine intake. Daily caffeine intake < 150 mg/d was not associated with statistically significant risk of childhood obesity. The association was not dependent on the source of caffeine. There was a dose-response relationship with increasing amount of maternal caffeine intake associated with further increased risk of obesity in offspring. The association was stronger for persistent obesity. There was no relationship with transitory obesity (not likely true obesity).
Conclusions: Maternal intake of high amount of caffeine during pregnancy is associated with increased risk of childhood obesity in offspring.

II-15 Associations of known genetic variants for adult body fat outcomes with measures of general and abdominal adiposity in children

EARLYNUTRITIONMEMBER

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Background: Various single nucleotide polymorphisms (SNPs) have been linked to adult body mass index (BMI) and waist-hip-ratio, explaining 1.45 and 1.03% of their variance, respectively. Whether these variants are associated with measures of general and abdominal childhood adiposity is unknown.
Aim: To study the associations of known SNPs for adult BMI and waist-hip-ratio with child general and abdominal adiposity at age 6.
Methods: This study included 4216 children participating in the multiethnic Generation R Study, a population-based prospective cohort study from fetal life onwards in Rotterdam, the Netherlands. Genome-wide association scans were available. BMI was calculated from measured height and weight. Total body and regional fat were measured using Dual-energy X-ray absorptiometry. Pre-peritoneal abdominal fat was measured using ultrasound. Multiple linear regression was performed.
Results: Of 28 SNPs previously associated with BMI in adults, four (rs2867125, rs1558902, rs7138803, rs713586) were significantly associated with child BMI. The 28 SNPs combined explained 2.4% of the variance in child BMI. Of 14 SNPs previously associated with adult waist-hip-ratio, one (rs6861681) was significantly associated with android/gynoid-fat-ratio (all P-values < 0.001). The 14 SNPs combined explained 0.6% of the variance in child android/gynoid-fat-ratio. None of the known SNPs were associated with child preperitoneal fat.
Conclusion: Only a minority of SNPs previously associated with adult body fat outcomes were associated with general and abdominal childhood adiposity measures. The adult BMI SNPs combined explained a relatively high proportion of the child BMI variance. These findings suggest that different genetic factors influence adiposity development during the life course.

II-16 Prenatal air pollution exposure: Associations with lower fetal growth and faster postnatal weight gain

EARLYNUTRITIONMEMBER

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Background: Air pollution exposure in late pregnancy inhibits fetal growth, but health implications beyond the perinatal period are unknown.
Methods: Among 2115 Boston-area infants in Project Viva, at birth and 6 months we assessed weights and (in a subset) lengths. We used spatiotemporal models to estimate third trimester residential exposure to black carbon (BC) and particulate matter (PM2.5) and geographic information systems to measure traffic density at late pregnancy address. We performed linear and logistic regression adjusted for sociodemographics. Analyses of postnatal outcomes were additionally adjusted for fetal growth and gestational age.
Results: Mean (SD, n) birth weight-for-gestational age (fetal growth) z-score was 0.17 (0.97, n=2114) and 0-6 month weight-for-length (WFL) gain 0.23 z-units (1.11, n=689); 17% (of n=1153) were obese (WFL ≥ 95th %ile) at 6 months. Of mothers, 67% were white and 16% obese. We observed lower fetal growth among infants in the highest (vs. lowest) quartile of residential third trimester BC (-0.16 units; 95% CI: -0.28, -0.05) and traffic density (-0.14 units; 95% CI: -0.25, -0.03). Infants in the highest (vs. lowest) quartile of residential traffic density had more rapid 0-6 month WFL gain (0.17 units; 95% CI: -0.06, 0.41) and higher odds of obesity (vs. WFL < 85th%ile) at 6 months (1.79; 95% CI: 1.10, 2.89). Results were similar for third trimester BC exposure (obesity OR 1.60; 95% CI: 0.98, 2.61). No outcomes were associated with PM2.5.
Conclusions: Infants exposed prenatally to higher traffic-related pollution may exhibit postnatal obesity in addition to lower fetal growth.

II-17 Adherence to a New Nordic Diet during pregnancy is associated with adequacy of fetal growth in the Norwegian Mother and Child Cohort Study (MoBa)

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Background and Objectives: Health effects of regional diets are increasingly being investigated in response to sustainability issues and public acceptance. Fetal growth strongly influences later health and development. The purpose of the present study was to investigate associations between adherence to a New Nordic Diet (NND) during pregnancy and fetal growth in the Norwegian Mother and Child Cohort Study (MoBa).
Methods: A diet score was constructed from a food frequency questionnaire (FFQ) completed around gestational week 22. The score comprised ten subscales addressing meals, Nordic fruits and vegetables, potatoes, oatmeal porridge, whole grain versus refined breads, foods from the wilderness (fish, game and berries), milk versus juice, and water versus soft drinks. For analysis participants were categorized as having either "low", "medium" or "high" NND-adherence. Infants were categorized as small (SGA), adequate (AGA) or large (LGA) for-gestational-age according to gender-specific birth weight cut-off values corresponding to the 10th and 90th percentiles as measured in 60 000 newborns born to nulliparous mothers in MoBa. Odds of being SGA or LGA (with AGA as reference) with high as compared to low NND-adherence were estimated with multivariable multinomial logistic regression.
Results: The study sample consisted of 66,597 women. Adjusted for age, parity, education, BMI, maternal height, smoking, exercise, diabetes, and energy intake, high as compared to low NND-adherence implied lower odds of SGA (OR: 0.92, 95% CI: 0.86, 0.99; p=0.025), but higher odds of LGA (OR: 1.07, 95% CI: 1.00, 1.15; p=0.048).
Conclusion: Higher NND-adherence during pregnancy was associated with enhanced fetal growth.

II-18 Ethnic disparities in general and abdominal adiposity at school-age. A multi-ethnic population-based cohort study in the Netherlands

EARLYNUTRITIONMEMBER

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We performed a population-based prospective cohort study in 5,244 children. At the age of 6 years, we measured height and weight. We calculated body mass index. Total fat mass and android/gynoid fat mass was assessed by Dual-energy X-ray absorptiometry (DXA) and pre-peritoneal abdominal fat mass was assessed by ultrasound.
Results: Overweight and obesity prevalences among Dutch children were 10.0% and 2.1%, respectively. Higher prevalences were observed among Cape Verdean (21.0% and 10.3%), Dutch Antillean (18.4% and 13.8%), Moroccan (20.6% and 7.7%), Surinamese-Creole (13.4% and 7.7%), Surinamese-Hindustani (12.3% and 6.2%), and Turkish (23.8% and 12.0%) children. In the models adjusted for non-modifiable factors, Moroccan, Surinamese-Hindustani and Turkish children had a higher, whereas Surinamese-Creole children had a lower total fat mass than Dutch children (all p-values < 0.05). Compared to Dutch children, android/gynoid fat mass was higher in Surinamese-Hindustani and Turkish, and pre-peritoneal abdominal fat mass was higher among Moroccan, Surinamese-Hindustani and Turkish children (all p-values < 0.05). Modifiable factors in pregnancy additionally explained 15% of the ethnic differences in childhood total and abdominal fat, whereas modifiable factors in childhood did not explain any of these associations.
Conclusion: All ethnic minority groups had higher risks of overweight and obesity than Dutch children. Our results suggest that Moroccan, Surinamese-Hindustani and Turkish children have an adverse body fat profile, whereas Cape Verdean, Dutch Antillean and Suri-

namese-Creole have a beneficial body fat profile. Pregnant women might be a target group for preventive strategies focused on reduction of ethnic disparities in childhood adiposity

II-19 Long-term effects of prenatal supplementation with 5-methyl-tetrahydrofolate on the offspring`s attention system at 8 years

EARLYNUTRITIONMEMBER

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Attention Network test and EEG recordings, at 8 years of life were used in 117 children from the NUHEAL study, to analyze long-term effects of prenatal supplementation with fish oil (FO), and/or 5-Methyltetrahydrofolate or placebo on children attention. We used the Attention Network Test, designed to assess conflict resolution abilities (executive function), readiness to respond (alerting) and orienting. Reaction times (RT), and error percentages (EP) were the dependent variables in two 2 (FO, between subjects) x 2 (5-MTHF, between subjects) x 3 (Flankers: congruent, incongruent, neutral) ANCOVA. Similar analysis was done for alerting and orienting data. We observed significant interference differences between groups for RT, $p< 0.03$. The 5-MTHF group showed less response conflict than the remaining groups (all $p< 0.05$). For errors, we only observed more EP for incongruent than for congruent or neutral trials, $p< 0.05$. Significant effects of the FOx5-MTHF interaction were observed for the ERP differences between congruent and incongruent flankers. ERP differences were larger for the 5-MTHF group (all $p< 0.03$). According to sLORETA, this group showed also the highest mid-dorsal cingulate activation. No effects were observed on orienting, and only on RT for the alertness network. The 5-MTHF supplemented rather than FO and the combination of both improves the children ability to solve conflicts, their executive function. This advantage seems to be based on the activation of right mid-dorsal cingulate, a core area in the executive network.

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II-20 The mercury inheritance; does maternal consumption of seafood during pregnancy lead to mercury levels that may be harmful to the child?

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Background: The fetal period is a critical developmental stage, and exposure to low-level mercury (Hg) during this period of brain growth may have long-term subtle negative effects on neurodevelopment. Seafood intake during pregnancy is of interest owing to its suggested benefits from nutrients, and as a well-known route of exposure to Hg.

Aims: To examine the association between Hg exposure and language development in the Norwegian Mother and Child Cohort Study (MoBa).

Methods: The study sample consisted of 50,240 women. Dietary exposure was calculated from an Hg-database and a FFQ covering the first part of pregnancy. Language development was assessed by language grammar rating scales at age three. Multivariable regression models were used to explore associations between Hg exposure and language development.

Results: Median exposure to Hg was 0.15 µg/kg bw/week, and the mean seafood intake was 237 gram/week. Women in the 90th percentile of Hg exposure had an increased risk of having a child with language delay associated with motor influence, odds ratio (OR) 2.40 (95% CI 1.27,4.55) and a moderate delay in language OR 1,19 (95%CI 1.00,1.19)adjusting for maternal age, BMI, energy intake, parents education and income, parity, smoking and alcohol in pregnancy, folate and EPA intake, and visit to a hearing specialist.

Conclusion: There is an overall low level of Hg exposure in the cohort. The finding among those highest exposed to Hg is supportive to the hypothesis that chronic exposure to higher doses of Hg during prenatal development may be associated with suboptimal cognitive development.

II-21 Association of excessive weight gain during pregnancy with postnatal growth and childhood obesity up to 4 years of age

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Background and aims: Gestational weight gain (GWG) is known to be associated with fetal growth, however there are few studies examining its effects on body size in early childhood. Our objective was to estimate the association of GWG with offspring size from birth to 4 years of age.

Methods: The present study was conducted in 1102 mother-child pairs participating in the Mother-Child (Rhea) cohort in Crete, Greece. GWG was reported by the mother postpartum and classified according to the 2009 Institute of Medicine (IOM/NRC) recommendations. Offspring's weight and height were measured at birth, 2 years and 4 years of age. In addition, waist circumference and four skinfold thicknesses were measured at 4 years of age. Multivariable linear and log poisson regression models were fit, adjusting also for potential confounders.

Results: Mean (SD) GWG was 14.1 (6.0) kg, with 42.8% of women gaining more weight than recommended. The percentage of overweight and obese children was 8% at 2 years and 22% at 4 years of age, according to International Obesity Task Force cut-offs. Women with excessive GWG had significantly higher risk of giving birth to a large for gestational age neonate infant [RR: 1.71, 95% CI: (1.24, 2.34)]. Excessive GWG, compared with recommended, was also associated with increased risk of overweight/obesity [RR: 1.41 95% CI: (1.01, 1.96)] and abdominal obesity [RR: 1.35, 95% CI: (1.02, 1.77)] at 4 years of age.

Conclusion: Excessive GWG, a modifiable factor, could be an important indicator of childhood obesity at early ages.

II-23 Body composition of preterm infants using air displacement plethysmography during the first weeks of life

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Background: Inadequate nutrition during the postnatal period may be associated with growth restriction, inappropriate accretion of lean and fat mass, poor neurodevelopment, and cardiovascular and metabolic diseases in later life. Tailoring nutrition to promote optimal growth requires monitoring of body composition (BC). Preterm infant BC could be used to guide nutritional strategies. Reference data of preterm infant BC is lacking.
Aim: Establish longitudinal reference data of preterm infant BC and growth using air-displacement-plethysmography at bedside.
Methods: Ongoing, single-centre, longitudinal, observational study of preterm infants. Inclusion criteria: 24-36wks gestational age (GA), infants without IV lines and stable off respiratory support for 7min, written and informed consent. Exclusion criteria: chromosomal or congenital abnormalities, hydrops fetalis. BC assessed by PEAPOD daily for the first 21days of life, then twice per week. Weight, length, head circumference collected once per week. Infants assessed from study inclusion to hospital discharge.
Results: A total 202 measurements of 82 preterm infants (GA:27-36wks) were performed. Percent fat mass (%FM) of preterm infants at postmenstrual ages 30, 31, 32, 33, 34, 35, 36 weeks were 9±2%, 8±4%, 9±3%, 11±5%, 14±6%, 13±7% and 12±8%. Fat-free mass and FM accretion occurred at different rates leading to an overall %FM increase after sufficient caloric intakes were established. Preliminary data suggests that %FM is not predicted by GA at birth. No infant experienced an adverse event relating to a measurement.
Discussion: Successfully established the infrastructure needed to routinely measure preterm infant BC at bedside in the NICU indicating PEAPOD´s feasibility for clinical use.

II-24 The impact of parental educational mobility on their adult offspring's overweight/obesity status: a study of three generations of Swedish men and women

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We investigated the impact of parents' educational mobility on their adult offspring's overweight/obesity. The Uppsala Birth Cohort Multigenerational Study is based on a representative cohort born in Sweden 1915-1929 (G1). Our sample included 5,122 women and 11,187 men who were grandchildren of G1 (G3) together with their parents and grandparents. G3's overweight/obesity (BMI≥25 Kg/m2) was based on self-reported, pre-pregnancy weight/height data for women before their first birth (average age=26 years), and measured weight/height at conscription for men (average age=18 years). G1's, G2's, and G3's highest educational attainment was obtained from registers and classified into low, medium, or high based on respective sample distributions. Parental (G2) educational mobility was defined as change in education between their own and their highest educated parent (G1), classified into 5 categories: always high/advantaged (AA), upwardly mobile (UM), stable-middle (SM), downwardly mobile (DM), and always low/disadvantaged (AD). We used hierarchical gender-stratified logistic regression models adjusted for G3's age, education, year of BMI collection, and lineage and G2's year of birth and income. Men whose parents belonged to UM, SM, and AD groups had higher odds of overweight/obesity compared to the AA. For women, results differed by lineage. Women whose fathers belonged to DM and AD groups had higher odds of overweight/obesity compared to the AA. Associations were only slightly attenuated on adjustment for G3's education and G2's income. Mothers' educational mobility was not associated with women's overweight/obesity status. This study provides evidence of intergenerational social determinants of overweight/obesity across more than two generations.

II-25 Thinness at birth and cardiovascular risk in childhood: The EU Childhood Obesity Project

EARLYNUTRITIONMEMBER

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Background: Our aim was to analyse the relationship between thinness at birth and cardiovascular risk in healthy infants born with appropriate weight.
Methods: This is prospective longitudinal study of 1678 children from 5 European countries, enrolled in the EU Childhood Obesity Project and followed-up to the age of 6 years (n= 657). Infants' birth weight and length were obtained from hospital records. Blood levels of triglycerides, LDL (LDLc) and HDL (HDLc) cholesterol were measured at 5.5 years and systolic (SBP) and diastolic (DBP) blood pressures at 6 years. According to their ponderal index (PI = weight [kg] / length [cm]^3) children were classified in three groups: thinner (PI ≤ 25th percentile), average (PI from 25th to 75th percentile), and fatter (PI > 75th percentile).
Results: At 5.5 years, infants born thinner showed significantly lower HDLc (47.8mg/dL), higher LDLc (108.8mg/dL) and triglycerides (79.7mg/dL) levels than infants born average or fatter (HDLc 56.5mg/dL and 55.3mg/dL; LDLc 97.8mg/dL and 95.6mg/dL; triglycerides 56.8mg/dL and 54.9mg/dL; all p≤0.001, respectively). At 6 years, infants born thinner showed significantly higher blood pressure than infants born average or fatter (SBP / DBP: (102.1 mmHg / 58.6 mmHg vs. 96.8 mmHg / 55.9 mmHg, both p ≤ 0.001; vs. 96.4 mmHg / 56.6 mm Hg, p < 0.001 / p = 0.081). Neither a difference in the lipid profile nor in blood pressure was observed between children born average and fatter.
Conclusion: Healthy appropriate-weight infants at birth with a low ponderal might have increased cardiovascular risk later in life.

II-26 The influence of late preterm birth on infant body composition at term corrected age

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Preterm birth and birth weight have lifelong implications for an individual's metabolic health.Preterm infants born before 32 completed weeks of pregnancy have altered body composition when they reach term (>37 weeks gestation). As there is a dearth of body composition data on late preterm (32-37 weeks gestation) infants, we hypothesized that they would similarly have altered body composition at term.

Infants born between 32-37 weeks gestation were eligible for recruitment. Their body composition was measured at term corrected age. Term infants (37-40 weeks gestation) whose body composition was measured using the PEA POD Infant Body Composition System (Cosmed, Rome, Italy) prior to hospital discharge served as study controls. Both groups of infants had anthropometric performed. The study was approved by the research ethics committee in the CWIUH and informed consent was obtained from the parents of all infants.

53 late preterm infants and 134 control infants had body composition analyzed at term. Preterm infants had a mean gestation of 34.6 weeks (SD 1.17) and birth weight 2.21kg (SD 0.4). Term control infants had a mean gestation of 39.7 (SD 1.35) and birth weight of 3.54kg (SD 0.5). Preterm infants weighed less at term (3.22 vs3.41kg p=0.02), with reduced fat free mass (2.74 vs 3.02kg p< 0.001) and increased fat mass (0.47 vs 0.39kg p=0.02) when compared with term born controls.

Though late preterm infants at term are lighter than control term born infants, they are more adipose. This raises concern for a negative metabolic impact and resultant lifelong health disparities.

II-27 Raising children with bovine metabolism. Follow-up study from Russia

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Background: The results of a survey conducted in Nizhny Novgorod, Russia in 2001 had revealed a low prevalence of exclusive breastfeeding and high incidence of whole cow´s milk feeding in infants.

Objective of the follow-up: To evaluate consequences of whole cow´s milk feeding in infancy on Body-Mass Index (BMI), blood pressure (BP) and glucose-insulin metabolism.

Methods: Case-control cohort analysis of 79 children, aged 6 years (74.95±17.8 months), recruited from a clinical population (n=436) who had participated during infancy in the 2001 feeding practice survey. Participants were divided into 2 groups according to type of feeding in infancy: those breastfed for a minimum of 9 months.

(BF; n=36), and those who were fed with whole cow´s milk during the first year (CM; n=43). We measured BMI, BP, fasting and 2-hour glucose and insulin levels following an oral glucose test.

Results: There was a clear trend separating BMI between the groups, beginning at 6 months and persisting through the most recent measurement (6 years) at which time the difference had become 1.3 times higher (β=1.697, p=.003). CM children showed higher systolic and diastolic BP (99.58 vs 93.39 mm Hg, p< 0.001; 68.23 vs 63.67 mm Hg, p=0.003), and a significant upward trend in 2-hour insulin (18.5 vs 9.52 mcIU, p=0.049).

Conclusions: These findings suggest that dietary patterns in infancy have immediate effects into toddlerhood and later. Cow´s milk feeding in infancy may predispose children to increased body mass, BP and insulin resistance.

II-28 Effect of maternal obesity and gestational diabetes on offspring`s neurodevelopment in relation to changes in placental gene expression

EARLYNUTRITIONMEMBER

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Objectives: To analyze if the placental expression changes of genes involved in the regulation of brain development in obese and diabetic pregnant women.

Methods: 120 infants, participants in the PREOBE study* were included in this analysis, which were born to: Healthy normo-weight (n:48), Overweight (n:27), Obese (n:13) and pregnant women with Gestational Diabetes (GD) (n:32). The offspring were neuropsychological examined using the Bayley Scales of Infant and Toddlers Development, (Bayley III) at 6 and 18 months of life. Statistical analysis was performed using SPSS Inc., version 20.0.

Results: No significant differences were shown in PPARG and IRS1 placental expression in the different groups. AMPK and P70S6KB1 were down-regulated and MTHFR was up-regulated in the placenta of GD mothers. At 6 months, Language Composite Score was higher in babies with higher MTHFR up-regulated levels (OR: 1.620; IC: 1.101-2.385); Motor Composite Score were positive related to a higher level of AMPK up-regulated at 6 months (OR: 2.516; IC: 1.167-5.422) and to higher level of IRS1 up-regulated at 18 months (OR: 1.889; IC: 1.009-3.537). Babies born to obese and GD mothers with higher levels of P70S6K up-regulated showed higher Language Composite Score at 6 months (P=0.018) and at 18 months (P=0.042). Babies born to obese mothers with higher level of AMPK up-regulated showed higher Cognitive Composite Score at 18 months of life (P=0.037).

Conclusion: Our results show that GD influences placental gene expression levels of genes involved in the regulation of brain development.

II-29 Identifying trajectories for healthy postnatal growth of preterm infants

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Introduction: Postnatal loss of extracellular fluid shifts growth trajectories to a percentile below that in-utero. Growth of preterm infants should follow intrauterine rates. Which "new" trajectory a preterm infant should adjust to after completed postnatal adaptation is unknown.

Objective:

1) To develop a model for postnatal growth trajectories of preterm infants by characterizing growth of such infants which required only minimal postnatal support;
2) to predict trajectories for healthy postnatal growth in any given infant.

Methods: Inclusion criteria: infants with (A) 30-35 and (B) 24-29 weeks GA, admitted 2008-2012 to participating hospitals. Exclusion criteria: (A)+(B) maternal diabetes/substance use, nosocomial sepsis (positive blood culture until day of life (DoL) 21 (A) nCPAP>3 days, not on full enteral feeds by DoL 10, (B) mechanical ventilation on DoL>3, FiO2≥0.3 within first 21 DoL, NEC>stage 2, IVH>2, PVL. Models to predict body weight trajectories on DoL 14&21 were developed.

Results: 890 infants were eligible of 6915 meeting inclusion criteria. Infants had maximum weight loss by DoL 5, regained birth weight by DoL 11 and showed stable growth parallel to intrauterine percentiles during DoL 7-21. Surprisingly the new trajectory was independent from GA with a z-score difference from birth of (A) -0.96±0.75 and (B) -0.88±0.67 at DoL 14. Linear regression models predicted weight at DoL 14 (R^2=0.88) and 21 (R^2=0.82).

Conclusions:

1) The study provides robust estimates of ideal postnatal growth trajectories for preterm infants.
2) The impact on long-term outcome using these trajectories for nutritional adjustment needs to be assessed, ideally in an RCT.

II-30 Birth weight in relation to sperm parameters in idiopathic subfertile men

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Introduction: Environmental factors and body composition may affect fertility. Foetal programming of metabolic diseases is a well-established concept but little is known about maternal prenatal environment and fertility of the offspring. As it is difficult to retrospectively assess in utero nutrition, birth weight may be used. Few animal studies have demonstrated that abnormal fetal growth is associated with impaired gonadal development.

Material and methods: Data from 75 men recruited within the ALIFERT study (clinical trial) were recorded. They were partners of subfertile couples, presented a primary idiopathic infertility, attending our infertility centre. Anthropometric parameters were measured. Blood samples were obtained for metabolic dosages. Semen samples were collected, conventional semen parameters were assessed and sperm DNA fragmentation was measured with TUNEL assay.

Results: Birth weights in our population ranged from 2500g to 4500g (mean: 3457g). Birth weight inversely correlated with total sperm count (p=0.0034) after adjustment for age and tobacco. Also a significantly positive association was observed between birth weight and LDL cholesterol (p=0.046).

Discussion: We present the first study demonstrating a significant association between male birth weight and total sperm count in a population of idiopathic subfertile men. Some data in women showed that high or low birth weights were associated with an increase of time to pregnancy. These results underline the importance of the in utero environment for male reproductive functions. Little is known about prenatal causes of subfecondity and epidemiological studies are necessary to assess the impact of maternal nutrition on offspring fertility and to understand mechanisms.

II-31 Early life stunting confers risk for adult hypertension in undernourished populations

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Populations where childhood malnutrition rather than obesity is predominant, disease risks in later life need to be studied in relation to stunting that represents chronic malnutrition. We examined risk of hypertension in 387 rural males above 20 yr age who were measured for anthropometry during childhood, adolescence and at young adult age in a community based study. At the age of 24 yr 33.9 % subjects had either high (≥130 mmHg) systolic blood pressure (SBP) or high (≥85mmHg) diastolic blood pressure (DBP) even in the absence of obesity. Boys who had high DBP were significantly ($p < 0.05$) shorter at 3+ yr compared to those having normal DBP. Boys with high adult BMI had higher risk of developing hypertension in the presence of stunting at 3+ yr (OR= 4.4; 1.27-15.15) and was specially high (OR=12.21; 2.93-50.90) for high DBP. Measurements on kidney size, volume and thickness (on 50 cases, 61 controls) showed that kidney volume was significantly smaller among subjects stunted in early life compared to non stunted (109.04± 26.4 cc Vs 115.06±19.6 cc; $p < 0.01$). It explained 20% variability in SBP (after adjusting for current BMI and age) in stunted subjects but regression was not significant among non stunted subjects. Early life stunting thus, may adversely affect size of kidney which in turn may be responsible for elevated adult blood pressure. The public health implications are that children should be monitored for height and awareness needs to be developed for prevention of excessive increase in BMI in later life.

II-32 Head circumference makes long-term outstanding fitting of brain size, cognition, and gray and white matter volume distribution

EARLYNUTRITIONMEMBER

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Head circumference (HC) measurements from birth to school age and the volumes of white (WMV), gray matter (GMV) and cortical surface area were performed in 80 children aged 9.14, participants in the NUHEAL Study, using structural MRI recordings. Cognitive assessment of the children was performed with the K-ABC at 6.7y. At age 10y, the inner brain total surface area ranged from 1135.8 to 1647.3 cm². Males' surface was larger than that of females. GMV ranged from 857 to 577 cm³, and being also larger in males than in females (716 vs 665 cm³). The same was observed for WMV (480 vs 443 cm³), and total brain volume (TBV, 1196 vs 1107 cm³). Family socio-economic status was related to GMV (r=0.27 p< 0.03) and TBV (r=0.25, p< 0.04) measures, but not to the surface area (r=0.20, p=0.10). HC at 4y correlated with intelligence score. More important, larger inner brain surface area, GMV, WMV and TBV were also associated to higher intelligence scores. Brain volumes closely matched the surface area results. At 4y, HC was strongly associated to GMV of bilateral anterior areas, including several frontal gyrus, anterior cingulate, bilateral temporal, encompassing temporal pole, superior and middle temporal gyrus and limbic areas, insular cortex, parahippocampal gyrus, hippocampus, amygdala, and small clusters in bilateral occipital areas.

Conclusion: HC, especially at 4y, makes a long-term outstanding fitting of brain size, cognition, GMV and WMV distribution in the brain.

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II-33 Percentage of commercial complementary food and fruit and vegetable intake in infancy and childhood - Results of the DONALD Study

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Objective: Sensory properties of foods given during infancy may influence later food acceptance and dietary intake. The range of taste experiences during weaning differs with respect to the preparation method of complementary food (CF), commercial or homemade. Thus, the aim of this study was to examine the association between the consumption of commercial CF (cCF) and fruit and vegetable (FV) intake during infancy, preschool and school age.

Methods: In total, 281 children of the DONALD Study with 3-day weighed dietary records at 0.5, 0.75 (T0), 3, 4 (T1), 6 and 7 years (T2) of age were included in this analysis. Percentage of cCF (%cCF) was calculated at T0; fruit, vegetable, and juice intake (in g/day) for every age group. Multivariate linear regression was used to analyse associations between %cCF and FV intake.

Results: At T0 49g/d of vegetables and 79g/d of fruits were consumed. Intake increased to 64g/d (T1) resp. 86g/d (T2) of vegetables and 112g/d (T1) resp. 119g/d (T2) of fruits. For boys, higher %cCF at T0 was associated with lower vegetable intake at T0 (p< 0.0001) and T1 (p=0.021) as well as lower total FV intake in all age groups (p< 0.035). For girls, higher %cCF at T0 was associated with lower vegetable intake (p< 0.0001) and higher juice intake (p=0.004) at T0.

Conclusion: The results of the DONALD Study indicate that the preparation method of CF may have an influence on FV consumption in infancy and at least for boys also in preschool and school age.

II-34 Maternal vitamin D status influences bone health in the newborns

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Background: Maternal vitamin D deficiency modulates fetal mineral bone acquisition and has influence on the neonatal skeletal development.

Objective: To determine the association between mother's vitamin D status and bone mineral density (BMD) in newborns at birth and at the age of one month.

Design: 128 healthy pregnant women and their term newborns were included in the "My Milk" project (www.moje-mleko.si/en), performed from May 2011 to June 2012. In the 32nd week of pregnancy, serum was collected and 25 (OH)D was measured by radioiodine (125I)-based radioimmunoassay. 25(OH)D was season-standardized (46° N altitude) and compared to existing recommendations. BMD was measured by quantitative ultrasound (Sunlight Omnisense Premier) on right mid-tibia in the first 48 hours after birth and at the age of one month; low BMD was defined as Z score -1.5 for age, weight and sex.

Results: The mean serum 25(OH)D concentration of pregnant women was 75.4 nmol/L; in less than half (45.9%) women serum concentrations of 25(OH)D were in the recommended range.The mean Z score of BMD in newborns at birth was -0.2; the values were in the normal range in 67% of newborns. Spearman's correlation coefficient showed a significant correlation between maternal 25(OH)D and BMD in newborns at birth (p=0.003), while there was no correlation at the age of one month (p=0.167). Mothers with high levels of 25(OH)D tended to have newborns with higher BMD at birth (p=0.001).

Conclusion: Our study provides the evidence of correlation between maternal 25(OH)D status and early infant BMD.

II-35 Postpartum maternal plasma adiponectin, but not leptin, is related to neonatal fat mass

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Introduction: Increased plasma leptin and reduced adiponectin are related to numerous metabolic disturbances and increased fat mass in adults. Recently, studies have shown that leptin and adiponectin may play a role in fetal growth. Neonatal fat mass may be important for prediction of health and disease later in life and it has been shown that neonates born to obese mothers have increased fat mass when compared to normal mothers. Our aim was to investigate if maternal plasma leptin and adiponectin are associated with neonatal fat mass.

Methods: 215 healthy women were selected after delivery from a maternity in São Paulo, Brazil. Maternal blood serum was collected 24-72hs after delivery for leptin and adiponectin determinations by enzyme linked immuno sorbent assay (ELISA). Maternal body composition was assessed by bioelectrical impedance using InBody 370 (Biospace, Korea). Several neonatal anthropometric measurements were assessed 24-72hs after birth and body composition was measured by the PEA POD (Cosmed, USA).

Results: In a multiple regression analysis model, it was found that maternal plasma adiponectin (p=0.04), maternal pre-pregnancy body mass index (p=0.004) and gender (p=0.007) were associated with neonatal fat mass.

Conclusion: Postpartum maternal fasting plasma adiponectin was associated with neonatal fat mass. This research seems to confirm animal studies that show the importance of adiponectin to neonatal fat deposition and placental nutrient transport. Cohort studies needs to be conducted to verify if there is a causal relationship between maternal serum adiponectin and neonatal fat mass.

II-36 Pregnancy outcomes following excessive gestational weight gain in an obese pregnant cohort

EARLYNUTRITIONMEMBER

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Objectives: Excess gestational weight gain (GWG) and maternal obesity increase the risk of adverse pregnancy outcomes. The objective of this study is to describe GWG patterns among obese pregnant women and to identify maternal factors and pregnancy outcomes associated with excessive GWG in obese pregnancy.

Methods: This prospective observational study recruited 128 pregnant women with a body mass index (BMI) of 30.0-39.9kg/m2 based on measured weight at first antenatal visit. Weight gain was monitored through pregnancy and ordinal logistic regression assessed the risk of various outcomes associated with GWG below, within or above the Institute of Medicine (IOM) recommendation of 5-9kg.

Results: The mean total GWG of the entire population was 10.2kg (SD 5.9) and 76 women (59%) exceeded the IOM guideline. Excess GWG was associated with younger maternal age, lower BMI and lower self-reported physical activity levels. Adjusting for BMI and age, women with GWG below or within the IOM guidelines had a significantly reduced risk of caesarean delivery (OR=0.42; CI 0.19-0.96), postpartum haemorrhage (OR=0.27; CI 0.09-0.80) and birthweight >4kg (OR=0.34; CI 0.13-0.91). However, these women also appeared to have an increased risk of gestational diabetes (OR=3.61; CI 1.40-9.32).

Conclusion: Excess GWG among obese pregnant women is highly prevalent, increasing the risk of several adverse pregnancy outcomes, and those of younger age with poor physical activity levels may be at highest risk. The observed inverse association between GWG and gestational diabetes risk may be explained by the stronger influence of pre-pregnancy obesity on maternal glycaemia, rather than GWG.

II-37 Physical activity attenuates the negative effect of low birth weight on leptin levels in European Adolescents; The HELENA Study

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We examined whether physical activity (PA) influences the association between birth weight and serum leptin in adolescents. The study comprised a total of 538 adolescents (315 girls), aged 12.5 to 17.49 years, born at term (≥37 weeks of gestation). We measured serum leptin levels and time engaged in moderate-vigorous PA (MVPA) by accelerometry. There was an interaction effect between birth weight and meeting the PA recommendations (60min/day MVPA) on leptin levels in girls (P=0.023) but not in boys (P=0.809). Birth weight was negatively associated with leptin levels in girls not meeting the PA recommendations (i.e. more than 60 min/day of MVPA) (ß= -0.096, P=0.009), whereas no significant association was observed in those meeting the PA recommendations (ß: -0.061, P=0.433). In conclusion, Meeting the PA recommendations may attenuate the negative effect of low birth weight on serum leptin levels in European female adolescents.

II-38 Serum leptin in infants in the first period of life and body mass index in childhood: A follow up study

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Background: Leptin is present in breast milk and plays a role in regulating appetite and food intake, affecting body composition. Cross-sectional studies have shown higher leptin serum levels in breast-fed (BF) infants than formula-fed (FF) ones in early infancy but the relationship with childhood obesity is already unclear.

Aim: To evaluate serum leptin concentration in infants according to kind of feeding before weaning and to investigate its possible relation with body mass index (BMI) after 9 years.

Methods: Between 2012 and 2013, we followed up 93 participants, who were previously involved in a clinical research between 2003 and 2005 aimed to detect serum leptin in early infancy. We evaluated weight, length, BMI in childhood and its possible relation with serum leptin levels in infancy. The data are expressed by median and interquartile range (IR). Multivariate analysis was conducted using multivariate linear regression model with BMI at recruitment as independent variable.
Results: In the follow up sample (n=93; mean age 9 years, SD 1.39) BF infants had a significantly higher leptin concentrations [n=50; 2.7 (2.8) ng/ml] than FF infants [n=43; 2.1 (1.8) ng/ml] ($p< 0.05$). BMI in childhood was significantly higher in FF infants than BF ones ($p< 0.001$). We observed that infants with a lower serum leptin level in infancy have a greater value of BMI in childhood ($p= 0.009$).
Conclusions: These findings support the possible role of leptin in infancy in obesity prevention confirming the protective effect of breastfeeding. Further investigation is required to confirm our observations.

II-39 Dietary polyphenols are available to newborns through breast milk feeding: A pilot study

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Human breast milk is an optimal food for newborns, supplying nutrients and minor compounds such as vitamins, micronutrients, and microconstituents essential for their development and health. The large body of epidemiological and clinical studies showed that dietary polyphenols play an important physiological role in human health. However, it is not clear till which extent these bioactive compounds are on the "menu card" of breast fed children. To address the accessibility of the dietary polyphenols to a newborn, determined by dietary intake of a lactating mother, we planned: (i) to evaluate the bioavailability of polyphenols in the breast milk of lactating mothers after acute dietary consumption of a polyphenol (catechin) rich dark chocolate; and (ii) to address whether the polyphenol metabolites could be detected in breast milk and could be related to dietary habits of breast-feeding mothers under uncontrolled free-living conditions. SPE-UPLC-MS/MS methodology was applied for direct evaluation of catechin metabolites in collected breast milk samples. Dietary habits of free-living lactating mothers (n=11) and two volunteers were monitored and polyphenol content was estimated. The kinetics of several principal host (epicatechin) and some microbial (valerolactones) phase II (glucuronides and sulfates) chocolate derived catechin metabolites was monitored in breast milk samples of both volunteers in correspondence to elsewhere reported data for plasma and urine. Some of these catechin metabolites were eventually detected in the breast milk samples belonging to free-living subjects. However, to be able to associate the dietary consumption of polyphenols at free-living conditions to the detected metabolites larger study is required.

II-40 Length normalized indices for fat mass and fat free mass for preterm and term infants during first 6 month of life

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Introduction: Neonatal body composition (BC) is related to lifelong morbidity. BC is not proportional to body length. BC data as percentages cannot be employed for comparison between neonates with different body length. Length normalized reference data of fat mass (nutritional status) and fat-free mass (body constitution) is desirable.
Objective: To develop fat mass/length2(FMI) and fat-free mass/length2(FFMI) for postmenstrual age in preterm and term infants during the first 6 months of corrected age.
Methods: The data (n=853) are from our recent 4 longitudinal studies, 396 preterm (22-36wks) and 133 term were analyzed. Time points for measurement were: 1)after reaching full enteral feeding, 2)at term, 3)two further time points until a maximum of 6 months of corrected age. DXA fat and fat-free mass was measured (QDR1500; Hologic) and considered as independent data points.
Results: Nutritional status expressed as median FMI for preterm increased from 0.7kg/m2 at 30wks to 2.1, 4.0, 4.3kg/m2 at 40, 52, 64wks, while term measured 1.7, 4.5, 5.8kg/m2 respectively. Body constitution developed until term age: median FFMI(preterm) increased between 30 and 45wks (7.8 to 11.5kg/m2) but remained stable thereafter (11.4 and 11.2kg/m2 at 52 to 64wks) whereas FFMI (term) remained stable throughout tested time points (11.0±0.1kg/m2). For preterm and term, length increased at same rates during first 6 months (0.76cm/wk,R2 =0.7). Preterm were consistently shorter than term infants.
Conclusions: This study provides large dataset for length normalized BC indices. Results highlight importance of optimal nutrition in preterm infants while body constitution is determined prior to term age.

II-41 The influence of maternal body composition on neonatal body composition

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Epidemiological studies suggest that obese women are more likely to have macrosomic babies. Much of this evidence is based on maternal body mass index (BMI) and infant birth weight. The link between maternal and infant body composition has not been well described. White European women with a singleton pregnancy were recruited after sonographic dating in the first trimester. Maternal body composition was measured using 8-electrode bioelectrical impedance analysis(Tanita). The body composition of term infants was measured within three days of delivery using air displacement plethysmography (PEAPOD).
Data from 310 mother-infant pairs were analysed. The mean maternal age was 29.4 years and the mean BMI was 26.2kg/m2. 22% (n=70) were obese (BMI >30kg/m2). Mean birth weight was 3.52kg and gestational age was 39.9 weeks. Women in the highest quartile of fat mass did not have heavier babies than women in quartiles 2 and 3 (3.70kg vs 3.57kg, $p = 0.09$). However, infants born to mothers in the lowest quartile of maternal percentage fat had a mean fat percentage of 9.7% compared to 14.0% in those born to mothers in the highest fat percentage quartile ($p < 0.01$).
BMI and birth weight are crude markers of adiposity. This study shows that birth weight is influenced more by maternal fat free mass than fat mass. However infant adiposity is influenced by maternal fat mass. The influence of maternal adiposity on infant adiposity cannot be accurately assessed by birth weight alone.

II-42 Early postnatal BMI adaptation is regulated during fixed time periods and mainly depends on maternal BMI

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We investigated whether there are critical time periods which influence the course of BMI during the first 6 years of life. From 5,433 children who participated in preschool examinations those 212 children were selected who crossed the BMI percentiles as a result of an extreme postnatal BMI rise (from < 10th to 90th percentile) or fall (from >90th to < 10th percentile) or who have persistently low or high BMI both at birth and at the age of 6 years. Forty children with a BMI close to the 50th percentile both at birth and age 6 years served as controls. The courses of weight, height and BMI during the first 6 years of age were assessed. To identify influences connected with BMI development, we investigated genetic, social, nutritional and other factors proceeding from the mother during pregnancy. Finally completed data sets of 57 children were available. Our study shows that during two critical time periods a significant move toward low or high BMI takes place among the groups: in early infancy from ~0.5 to 1.5 years and again from 5 to 6 years. At the age of 1.5 years the final state of BMI is already fixed in all study groups. Mothers of overweight 6-year-old children are overweight, whereas mothers of underweight 6-year-old children have a below-normal BMI. All other investigated factors only had a minor influence on postnatal BMI development. We conclude that postnatal BMI development follows a fixed genetic program and is mainly programmed by maternal metabolism.

II-43 Changes in beverage consumption habits from pre-pregnancy to early pregnancy among Norwegian women

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The present study explores the changes in beverage drinking pattern from pre-pregnancy to early pregnancy among Norwegian women.
Methods: Nulliparous women aged ≤ 18 years with a singleton pregnancy and a BMI ≥ 19, were consecutively recruited from April 2010 to January 2013 at primary health clinics in Southern Norway. At inclusion, in gestational week 16 (median, 9-20), 576 women reported how often they consumed various beverages at present, and in retrospect how often they drank the different beverages before they got pregnant. The answers were dichotomized into drinking ≥1 times per day and drinking < 1 times per day for all the beverages except alcohol which was dichotomized into drinking ≥ 1 times per week and drinking < 1 times per week. Changes in consumption of different beverages were analyzed with repeated measure analysis.
Results: The percentage of women reporting drinking milk (36% v. 42%), fruit juice (15% v. 23%) and water (85% v. 92%) daily or more frequent all increased significantly from pre-pregnancy to early pregnancy ($p < 0.001$ for all items), while the percentage of women who reported at least daily consumption of sugar sweetened beverage (9% v. 6%, $p=0.002$), artificial sweetened beverage (14% v. 10%, $p=0.001$) and coffee (42% v. 11%, $p < 0.001$) all significantly decreased. Pre-pregnancy, 10% reported drinking alcohol at least once weekly, whereas no one reported drinking alcohol weekly or more frequent in pregnancy ($p < 0.001$).
Conclusion: There is a significant change in beverage consumption habits from pre-pregnancy to early pregnancy among Norwegian women.

II-44 Seafood intake, n-3 fatty acid levels and iodine status in pregnant Norwegian women. Preliminary results from a longitudinal population study

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Seafood is a unique dietary source of the marine n-3 fatty acids, high quality proteins, vitamin D and iodine, and the recommendation is to eat 300 to 450 grams of seafood weekly also during pregnancy. The marine n-3 fatty acid, eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA) plays an important role in the growth, development and structure of the brain. Adequate iodine nutrition during pregnancy is needed for the production of thyroid hormones. Therefore, both low levels of marine n-3 fatty acids and iodine deficiency have been associated with impairments of child neurodevelopment. In this study, pregnant women were enrolled at nine different well-baby clinics (n=1041). The Little in Norway cohort is an ongoing longitudinal study of infant developmental pathways from pregnancy to age 18 months and the data collection will be finished late autumn 2014. In the present abstract results from 244 pregnant women will be presented. Dietary intake was assessed using a web-based, semi-quantitative food frequency questionnaire, and non-fasting blood- and urine samples were collected in gestational weeks 26-32. The women reported consuming seafood for dinner 1.3 ± 0.9 times per week and seafood as spread 1.3 ± 0.9 times per week. The level of EPA, DPA and DHA was 17 ± 11, 39 ± 12 and 151 ± 35 µg/g red blood cells, respectively and the omega-3 index (sum EPA + DHA) was 7.5% ± 1.9% of total fatty acids. Results regarding iodine status are pending and will be presented.

II-45 Long-term effects of armed conflict induced growth impairment during early life on growth and height: A longitudinal community study in northern Uganda and Guinea-Bissau

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Background: Chronic malnutrition in early life can lead to childhood stunting, shorter adult attained height and is believed play a crucial role in adult obesity and cardiovascular disease risk. However, limited data are available from sub-Saharan Africa, where the developmental origin of health and disease theories may apply differently. Populations affected by armed conflict are exposed to multiple stressors to growth. Preliminary findings from northern Uganda indicates unexpected sex-differential effects of exposure to conflict during early life on the risk of being short statured, suggesting that males are more vulnerable than females. However, people born during the conflict had not yet reached their final height at the time of the study.
Aim: Examine the long-term, including sex-differential-, effects of conflict induced impairment of nutrition and growth during early life on later growth patterns and final height in two different conflict cohorts: a long lasting armed conflict in northern Uganda and a shorter armed conflict in Guinea-Bissau.
Methods: The study will be conducted in 2014-17 within two health and demographic surveillance systems (HDSS); Gulu HDSS, Uganda and Bandim Health Project, Guinea-Bissau. Outcome measurements: adult attained height, biannual measurements of children and adolescents (< 23yrs), leg-length, weight, arm-, waist- and hip-circumference.
Output: The study will provide unique growth monitoring data beyond childhood, which is rare in sub-Saharan Africa, and build a foundation to study early life exposures, growth, height and nutrition and chronic diseases in later life in low-income settings, including how foetal programming theories apply in different African settings.

II-46 Maternal CG PRO12ALA PPAR γ2 polymorphism and infant neurodevelopment scores at 18 months of age

EARLYNUTRITIONMEMBER

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Objectives: To determine the influence of mothers´ Pro12Ala PPARγ2 gene polymorphisms on offspring neurodevelopment at 18 months of life.
Methods: A total of 138 mother-infant pairs recruited in the PREOBE study were included. Mothers and infants were genotyped for Pro12Ala PPARγ2 (Applied Biosystems, Foster City, CA-USA). Neuropsychological assessment was performed using Bayley Scales of Infant and Toddlers Development, Third Edition. Pre-conception BMI, mother´s age, diabetic condition, parity, smoking, alcohol consumption, placental weight, neonatal anthropometry, gender and type of feeding during early life were considered as a confounders. SPSS version 20.0 was used for statistical analysis.
Results: 118 women (85.5%) had major CC genotype and 20 women (14.5%) showed the heterozygous genotype of CG. No homozygosis was found in the mothers´ group. Babies born to mothers with CG Pro12Ala PPAR γ2 polymorphism had higher birth weight (p=0.036). At 6 months of age, no differences in neurodevelopment were observed between babies born to CC or CG mothers. At 18 months, in the cognitive domain, both the composite and the scaled scores were significantly lower in the offspring of CG mothers (p=0.006). Logistic regression analysis demonstrated that CG mothers have 13% of risk to have babies with lower cognitive development at18 months (IC: 0.028-0.606). Scaled Receptive Communication, Scaled Fine Motor and Motor Composite scores resulted significantly lower (p=0.020, p=0.042, p=0.013, respectively) for babies born to CG mothers at 18 months.
Conclusion: The present study suggests that Mothers´ PPARg rs1801282 CG polymorphism plays a negative role on their offspring neurodevelopment scores at 18 months.

II-47 Sex differences in response to maternal long-term nutrition

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Maternal long-term nutrition may contribute to fetal programming of later life diseases. Placenta is a plastic organ that reflects both maternal nutritional status and fetal demands of nutrition. Recently, placenta has been linked to fetal programming. Unlike other places, newborn boys are smaller than girls in Baish city, Saudi Arabia. In order to investigate the associations between maternal long-term nutrition (as reflected by mother´s height and head circumference) and birth measurements we studied 321 pregnant women, their babies and placentas.
Boyes were significantly smaller, shorter and had smaller chest circumference compared to girls but had larger head circumference. Placental weight in boys was similar to girls, but feto-placental ratio was greater in boys. Placental breadth and length were larger in girls. Boys´ placentas were significantly thicker and had more cotyledons than in girls. Mothers of boys were shorter and their head was smaller but their BMI was greater than mothers of girls.
We conclude that, within Saudi Arabia, there are geographical and sex differences in placental dimensions. In the adverse circumstances of Baish, linked to the mothers' short stature and small head, boys were smaller at birth than girls. Boys tended to have larger head circumferences and smaller chest than girls. This led to the conclusion that boys tend to trade off visceral and soft tissue development in order to protect brain growth. Boys may have compensated for under-nutrition by increasing the depth of spiral artery invasion rather than by recruiting additional spiral arteries.

II-48 Non-HDL-Cholesterol is associated with obesity in prepubertal children

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Objective: To evaluated the association between the Non-HDL-cholesterol with plasmatic concentration of cysteine, homocysteine,

glucose, nutritional status and waist circumference in prepubertal children.
Methods: In cross sectional study with 695 prepubertal children (age: 6-11 years old) to public school of Santo Andre (Sao Paulo/Brazil) was collected: weight, height and waist circumference which were used to calculated z-score of body-mass-index (ZBMI, cutoff: obesity > 2.0; WHO, 2007) and waist circumference/height (cutoff: inadequate > 0.5). After fasting 12 hours were collected 10 mL of blood for determination of lipid profile (HDL-c, LDL-c, cholesterol total and triglycerides), serum glucose (cutoff: inadequate > 100 mg/dL), plasmatic concentration of homocysteine and cysteine (cutoff: > 90th Leite NP, et al 2013). The lipid profile was used to calculate de NHDL-c (total cholesterol - HDL-c, cutoff: inadequate > 145 mg/dL, Dai S et al, 2013). Statistics: logistic binary regression.
Results: The median of age was 8.8 y (6.5,11.5). NHDL-c median was 121.7 mg/dL (29.9,234.1) and 140/674 (20.1%) was inadequate, without difference between gender. In multivariable analysis just obesity was associated with inadequate NHDL-c (OR = 2.04, CI 95% 1.3-3.2).
Conclusions: Obesity increases at twice the risk of inadequate concentrations of NHDL-c in prepubertal children. The research of early atherosclerosis markers in young children is important in the current pediatric obesity epidemic.

II-49 Effect of maternal physical characteristics on infant's growth pattern during the first year of life

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Background: Data on how maternal physical characteristics affect infant's growth pattern are lacking, therefore the effects of maternal pre- and during-pregnancy physical characteristics on infants' growth in the first year of life were analysed.
Methods: Pregnant women and their neonates (N=145 pairs) participated in the study ("My-Milk" project; NCT01548313). Women's body height, mass before and at the end of pregnancy, and infants' body length, mass, and head circumference at birth and age of 1, 3, and 12 months were measured. Women's pre-pregnancy body mass index (ppBMI; kg/m2) and pregnancy mass gain (PMG; kg) were calculated and PMG was classified according to the ppBMI (PMG-ppBMI) as low, appropriate, or high. For infants, BMI and relative changes in physical characteristics were calculated. Respectively to women's characteristics, relative changes in infants' physical characteristics were compared by a repeated-measure-ANOVA.
Results: Over the first year of life, relative increases in infants' mass and BMI were smaller in those born to women with high PMG and PMG-ppBMI, but were not affected by mother's height or her pre-pregnancy mass. Similarly, relative length increases were smaller in those born to mothers with high PMG-ppBMI. Head circumference increased faster in infants of mothers, who were taller and had had high pre-pregnancy mass, but not of those, with high PMG and PMG-ppBMI.
Conclusions: The results suggest that infants' mass, BMI, and length in the first year of life are more affected by changes in mother's physical characteristics during pregnancy (intrauterine environment), while infant's head circumference by mother's pre-pregnancy characteristics (genetics).

II-50 Assessment of body fat percentage by using bioelectrical impedance analysis and its association with some anthropometric measurements

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Objective: Body fat percentage analysis with bioelectrical impedance analysis (BIA) is a simple measurement correlated with body mass indeks (BMI) and anthropometric measurements. Aim of this study is, to correlate body fat percentage with BMI, waist circumference, waist to height ratio, biceps and triceps skinfold thickness.
Methods: This is a cross-sectional, descriptive study. The questionnaire used in the study was applied to 120 female university students selected by random sampling method. The questionnaire includes general demographic variables and some anthropometric measurements of individuals. Bioelectrical impedance analyzer was used for analyzing body fat percentage (50kHz, 500A).
Findings: Among the attendants with mean age of 21.08±1.38 years 11 students (9.2%) were classified as underweight; 102 students (85.0%), normal weight and 7 students (5.8%), overweight. A significant correlation was observed between body fat assessed by BIA and BMI, waist circumference, waist to height ratio, triceps skinfold thickness, biceps skinfold thickness (respectively r : 0.570, 0.526, 0.412, 0.412, 0.294; $p < 0.01$).
Conclusion: BMI, waist circumference, waist to height ratio, triceps skinfold thickness, biceps skinfold thickness can be used as proxies to identify excess body fat in young adults when BIA is not available in the field.

II-51 Does low birth weight influence metabolic disease risk in adolescence?

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Introduction: Although recent studies have indicated preterm infants are prone to develop metabolic syndrome in adulthood, their mechanisms have been unclear. MicroRNAs (miRNAs) are noncoding RNAs which regulate gene expression at the post-transcription level and are involved in many metabolic homeostasis.

Objectives: To evaluate risk of low birth weight for development of metabolic syndrome in adolescence.

Methodology: This study consists of 13 very low birth weight (VLBW) subjects and 10 normal birth weight subjects. We collected the data of height, weight, body mass index (BMI), blood pressure, serum total cholesterol (T-CHO), HDL, LDL, TG, fasting blood sugar, insulin and GPT. Blood samples were collected from 23 participants (17-20 years old). MiRNAs expression in blood cells was compared between 8 VLBW subjects and 7 normal subjects using microarray. We compared these data with VLBW and normal subjects. Differences in demographic characteristics and clinical measures were examined by unpaired t-test. Statistically significant differences were identified at $P < 0.05$.

Results and discussion: Women's height of VLBW was shorter than normal subjects. Men of VLBW showed lower T-CHO and HDL than normal subjects. These findings indicate that low birth weight is a high risk of a lipid metabolic abnormality and this propensity has already started in adolescence. The levels of some miRNAs expression were correlated with serum HDL among all samples. These miRNAs may be a predicted marker of metabolic syndrome.

Conclusion: Metabolic syndrome due to low birth weight may begin in adolescence.

II-52 Investigation of the relationship between fat percentage obtained from bioelectrical impedance analysis and fat percentages calculated by various equations

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Objective: To investigate the relationship between fat percentage obtained from BIA and fat percentages calculated by various formulas of young women aimed in this study.

Subjects and methods: The study was carried out on 120 volunteer young women with a mean age of 21.08±1.38 between October 2012 and January 2013 at Gazi University Department of Nutrition and Dietetics. In this study, anthropometric measurements taken from individuals are body weight, height, waist circumference, hip circumference, triceps skinfold thickness, biceps skinfold thickness measurements. Anthropometric measurements were taken by the researchers with proper techniques.

Results: Mean body fat percentage of the individual obtained from BIA is 24.43±4.77 %. Body fat percentages calculated from the waist circumference, body mass index, triceps skinfold thickness is 26.20±2.20 %, 26.06±2.47 %, 27.74±4.50 %, respectively. A high correlation was found between total fat percentage obtained from BIA and the fat percentages calculated from the equations (Intraclass correlation coefficient = 0.75, Cronbach´s alpha = 0.751).

Conclusion: In this study, body fat percentage received from Tanita BC 480, a well known bioelectrical impedance analyzer, and total body fat percentage calculated by the equations was found to have consistency. Due to the limited access to bioelectrical impedance analyzers calculating body fat percentage with formulas can be considered to be practical. The same study can be carried out on men of the same age group.

Key words: Fat percentage, equations, anthropometry.

II-53 Comparable perinatal morbidites in the extremes of fetal growth - the power of programming?

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Background: Both extremes of abnormal fetal growth, namely growth restriction on one hand and fetal overgrowth on the other, have the propensity for many prenatal and neonatal adverse outcomes and are also being recognized as fetal origins of various adult diseases. Our aim was to compare perinatal morbidities of small (SGA) and large for gestational age (LGA) newborns with regard to general population of newborns.

Methods: In a retrospective study of 35 SGA and 35 LGA newborns inpatient charts were reviewed and data on fetal growth, perinatal and neonatal effects and neurological assessment of newborns were studied. The data was compared to the general population of newborns.

Results: Mothers of SGA compared to mothers of LGA newborns had more preeclampsia (p = 0,028) and more other adverse pregnancy outcomes (p = 0,025). The frequency of perinatal hypoxia, congenital anomalies, heart diseases, respiratory distress, hypoglycaemia, polycythemia and jaundice in SGA and LGA group was not significantly different and was higher in comparison to general population. LGA newborns had significantly more birth injuries than SGA (p = 0,009). Two thirds of SGA in comparison to one third of LGA had non-optimal neurological status and pathologic head ultrasound (p = 0,003; p = 0,004).

Conclusions: Both, SGA and LGA, have comparable and increased neonatal morbidity regarding the general population. Both extremes of fetal growth seem to be subjected to the similar programming reflected in the similar perinatal morbidities and maldevelopment and should therefore be carefully followed through the childhood to the adult age.

III - Mechanisms

III-1 Fetal gender determines the placental gene expression response to maternal obesity and voluntary exercise in rodents

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Background: The recent increase in obesity amongst pregnant women and associated adverse outcomes including gestational diabetes has led the development of interventions designed to reduce insulin resistance. These include a recommendation for increasing physical activity. Reports suggest that maternal obesity influences placental function. The influence of interventions in obese pregnant women on placental function is not known.

Objective: To investigate the impact of maternal obesity and physical activity on mRNA expression of genes involved in energy sensing, inflammation and lipid handling pathways in placentas from obese rodents. Since there is increasing evidence that "female" placentae show an exaggerated response to maternal stress signals in comparison to "male", we have compared responses in placentas from male and female fetuses.

Methods: Pregnant diet induced obese Sprague Dawley Rats (n=30) were allocated to Obese (Ob) or Obese-Exercise (Ob-Exx) groups. Ob-Exx dams were allowed access to a running wheel in the cage until termination and placental isolation at G20. Fetal sex was identified by sex determining region Y (SRY) and β-actin sequence amplification using PCR. To analyze placental gene expression, QPCR assays were applied and mRNA abundance was calculated using geNorm.

Results: The majority of genes examined were stable between sexes and experimental groups. However, mRNA abundance in "female", but not "male" placentae for IRS2, mTOR and TCF7L2 were significantly raised with exercise.

Conclusions: Up-regulation in genes involved in energy sensing displayed in "female", but not "male" placentae confirms the sexual dimorphic response to a suboptimal maternal environment that is modulated by physical activity.

III-2 Moderate maternal nutrient reduction induces extensive changes of cerebral gene transcription pattern and cerebral maturation in the baboon

Poster of Distinction

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In contrast to the beneficial effects of caloric restriction, even moderate dieting during pregnancy alters fetal brain development. We reported comprehensive changes of transcriptional activity and structural alterations of cell proliferation, establishment of neuronal network and myelinogenesis in the fetal baboon at mid-gestation after 30% global maternal nutrient reduction (MNR).

To determine effects of continuing MNR, 14 pregnant baboons received ad libitum or 70% of weight adjusted ad libitum diet at 0.16-0.90 gestation. Whole genome expression profiling of the fetal cerebral cortex was performed (Affymetrix). 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.

MNR resulted in 1519 differently expressed genes (390 up-regulated/ 1129 down-regulated genes). Gene ontological pathway analysis revealed 139 up-regulated and 321 down-regulated pathways. These gender-related transcriptional changes are related to cerebral developmental processes (including cell differentiation, neuronal network formation, cell communication, synaptic transmission and higher brain functions), cerebral metabolism, cellular homeostasis, stress response, and cell defense mechanisms including inflammatory pathways. MNR led to an increased number of migrating immature neurons and a reduced number of mature neurons in the cerebral cortex ($p < 0.05$) in parallel with reduced synaptic and fiber network density ($p < 0.01$) as well as reduced myelination ($p < 0.05$).

Cerebral transcriptional and structural adaptation to MNR occurs during the entire pregnancy and may contribute to alteration in brain function throughout life.

III-3 Effect of glycaemic dietary intervention during pregnancy on maternal body composition, metabolic status and placental gene expression

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Background: The increase in obesity amongst pregnant women and associated metabolic comorbidities including gestational diabetes (GDM), has led the development of treatments designed to improve insulin sensitivity. Evidence suggests reducing glucose content and glycaemic absorption rates in gestational diets may improve the metabolic dysfunction associated with GDM. Maternal obesity has been shown to modify placental function. The influence of these interventions on placental function with obesity is unknown.

Objective: To investigate the impact of changes in glycaemic load during gestation with maternal obesity on body compositions and metabolic profiles of mothers, and mRNA expression of genes involved in energy sensing, inflammation and lipid handling pathways in placentas from obese rodents.

Methods: Sprague Dawley Rats (n=24) were placed on a high fat diet for 6 weeks before mating. At G2 dams were allocated to low (HF-LGI), medium (HF-MGI) or high (HF-HGI) glycaemic index groups. Placentae were extracted at G20 and stored in RNA later. To analyze placental gene expression, QPCR assays were applied and mRNA abundance was calculated using geNorm.

Results: During gestation, no differences were exhibited in maternal body weights between groups. However, high GI mothers displayed increased adiposity and elevated plasma insulin, triglycerides and NEFAs. All placental genes examined were stable between the glycaemic groups except FATP4 which was increased in high GI dams.

Conclusions: A high GI diet during gestation exacerbated a poorer maternal metabolic profile with obesity and although gene expression appeared predominantly stable, further investigations in any potential morphometric and related placental modifications are required.

III-4 Oxidized components of frying oil ingested during pregnancy disturb vitamin A metabolism and are potentially teratogenic in mice

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We previously observed a higher incidence of congenital malformations in the fetuses of dams fed an oxidized frying oil (OFO)-containing diet during pregnancy. Since OFO is known to activate PPARα and modulate CYP450 enzyme activity and since some CYP450 enzymes are known to be involved in retinoid metabolism, we hypothesized that, during pregnancy, maternal ingestion of OFO, specifically the oxidized components (i.e. the polar fraction), modulates PPARα or aryl hydrocarbon receptor (AhR) transactivity, altering the metabolism of retinoic acid (RA). Pregnant C57BL/6J mice were divided into four groups which, from d1 (conception) to d18, were fed a diet containing 10 g/100 g of fresh soybean oil (SO, control), OFO or the non-polar (NP) or polar (PO) fraction of OFO. Reporter assays testing the transactivity of PPARα and AhR showed that free fatty acids from OFO, specifically the PO fraction, upregulated PPARα and downregulated AhR transactivity. Our results showed that the incidence of abnormalities in terms of gross morphology and skeletal ossification of the fetus was greatest in the PO fraction group, followed by the OFO group, both values being significantly higher than in the other two groups. Hepatic expression of genes encoding enzymes associated with RA synthesis and catabolism in dams and fetuses was differentially affected by PO fraction assault. We conclude that OFO-mediated teratogenesis is associated with disturbed RA metabolism in the dams and fetuses caused, at least in part, by modulation of PPARα and AhR transactivity by the oxidized components in OFO.

III-5 Polymorphism in leptin receptor gene influences maternal weight gain during pregnancy

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Objective: Weight gain during pregnancy is determined by many factors, however, there is still no clear evidence of the role of maternal genetics in pregnancy weight gain. We aimed to analyse if maternal genetic variation in a set of genes influences mother's weight change during pregnancy.

Material and methods: A total of 128 women from the PREOBE Study were included (mean weight gain during pregnancy was 9.87±5.81 kg, mean age 31.20±4.2 years, mean BMI before pregnancy 26.27±4.96). The following genotypes in candidate genes were analysed: ADRB3 T/C rs4994, GNB3 T/C rs5443, LEP19 G/A rs2167270, LEP2548 G/A rs7799039, LEPR G/A rs1137101, MC4R134 G/A rs12970134, MC4R313 T/C rs17782313, MC4R616 G/A rs2229616, MC4R633 G/A rs17700633, PPAR C/G rs1801282, UCP2 C/T rs659366. Hierarchical step-wise regression analysis was applied. In the first block the cofounders were entered into the model, and in the second block we entered all the polymorphisms studied using step-wise method, so that the model will retain only those, which would significantly predict the weight change.

Results: Out of the 11 studied polymorphisms, LEPR G/A predicted the weight change (b coefficient 1.4, p=0.023) among studied women, meaning that women with GA genotype had 1.4kg increased weight gain and women with AA genotype 2.8kg increase when compared to GG genotype, with confidence interval (C.I.) 0.2-2.7.

Conclusions: These results suggest that the LEPR G/A polymorphism influences weight change during pregnancy in our study sample, contributing to a higher maternal weight gain.

III-6 Postnatal programming with dietary lipid structure may protect against obesity through enhanced mitochondrial function in adipose tissue

EARLYNUTRITIONMEMBER **Poster of Distinction**

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Developmental programming of mitochondrial function in early life has been proposed as a potential underlying mechanism for later obesity and metabolic disease. The objective of the present study was to determine whether programming of body composition by postnatal exposure to a concept infant milk formula (IMF) containing large, phospholipid coated lipid globules (Nuturis®) (1), can be explained by altered mitochondrial function.

From postnatal day(PN)16 to 42, 12 male mice received Nuturis® (Concept) or standard IMF (CTRL) diet after which mice were challenged with a Western style diet (WSD, 20%w/w fat) until dissection at PN98. A reference group was included (REF), fed with AIN93-M from PN42-PN98. Citrate synthase (CS) activity, expression of metabolic genes and OXPHOS protein expression were analysed.

At PN98, relative protein expression of complex V of OXPHOS, indicator for mitochondrial capacity, was increased in the Concept group compared to the REF group (0.73 ± 0.11 vs. 0.41 ± 0.06, p< 0.05). CS activity, indicator for mitochondrial content, tended to be higher in the Concept group versus the CTRL group (p=0.08). Relative gene expression of uncoupling protein 3 and pyruvate dehydrogenase kinase 4 was decreased in the CTRL group compared to the REF group (p< 0.05), whereas the Concept group had intermediate levels. These results indicate that feeding with Nuturis® favours mitochondrial function in adipose tissue. Therefore, the higher mitochondrial content and capacity could underlie the protective effects of Nuturis® against excessive fat accumulation in adulthood.

(1) Oosting et al., Br. J. Nutr., 2013, [Epub ahead of print], 1-12.

III-7 The embryonic amino acid metabolism adapts to a diabetic environment

Poster of Distinction

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An adequate amino acid supply is essential for embryo development and fetal growth during pregnancy. As the embryo is highly sensitive to its surrounding milieu and vulnerable to dysregulations by external stimuli, we have investigated the influence of a maternal diabetes mellitus type 1 (IDD) on embryonic amino acid metabolism.

In female rabbits an experimental IDD was established by alloxan treatment. The amino acid concentrations were measured in maternal plasma and in preimplantation embryos. In plasma of diabetic mothers the concentrations of 12 amino acids were altered. Branched chain amino acids (BCAA) were elevated in maternal plasma and also in blastocyst cavity fluid. The expression of BCAA oxidising enzymes (Bcat2, Dbt) was determined by real time PCR. In adipose tissue of diabetic rabbits the expression of Bcat2 was enhanced. Embryos grown in a diabetic environment revealed an increased expression of Bcat2 and Dbt. They also had an elevated phosphorylation of mTOR and its downstream target S6K1.

To analyse the effects of L-leucine stimulation on mTOR signalling, we cultured day 6 blastocysts with L-leucine in vitro. L-leucine supplementation led to an increase in mTOR and S6K1 phosphorylation (30 min), indicating that the blastocyst is sensitive to L-leucine. Rapamycin, an inhibitor of mTOR, reversed this effect and S6K1 phosphorylation was inhibited.

Our findings demonstrate that maternal diabetes leads to enhanced BCAA concentrations and an altered BCAA metabolism in preimplantation embryos. It affects embryonic mTOR activation with likely changes in mTOR signalling.

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III-8 The effect of a short-term high-fat overfeeding on plasma levels of amino acids in young, healthy men with low or normal birth weight

Poster of Distinction

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Changes in plasma amino acid (AA) levels during overfeeding may modulate insulin secretion and/or action and could thereby impact the risk of developing type 2 diabetes (T2D). Low birth weight (LBW) subjects have an increased risk of developing T2D compared with normal birth weight (NBW) subjects when exposed to high-fat feeding. Here, we tested if this might be mediated by differential changes in plasma AA levels.

We used tandem mass spectrometry to investigate plasma levels of eighteen AA before and after 5-days high-fat overfeeding in young, healthy male LBW (n=20) and NBW (n=26) subjects. Subsequently, we studied whether alterations in AA levels were associated with changes in insulin secretion and/or action.

We observed no significant differences in plasma AA levels between LBW and NBW subjects, for either the control or high-fat diet. However, both birth weight groups displayed a highly significant increase in alanine level, and a decrease in leucine/isoleucine levels, after overfeeding. Additionally, NBW subjects showed a reduction in histidine and proline levels after overfeeding. Interestingly, the decrease in leucine/isoleucine and histidine levels was associated with an increase in insulin secretion after overfeeding, independent of birth weight. Furthermore, the decrease in proline level was associated with attenuated reduction in peripheral insulin sensitivity following overfeeding.

In conclusion, 5-days high-fat overfeeding influenced the levels and composition of plasma AA in a similar manner in LBW and NBW subjects. The down-regulation of certain AA in response to overfeeding could represent a physiological adaption, which potentially influences the risk of developing T2D.

III-9 Early long-chain polyunsaturated fatty acid intervention can prevent neuroinflammatory processes in the brain caused by an obesogenic diet later in life

Poster of Distinction

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Obesity represents a major global health problem that is associated with cognitive dysfunction. The aim of the present study was to investigate whether potential detrimental effects of an obesogenic diet on brain structure and function could be prevented by early intervention with ARA/DHA in a humanized model for hyperlipidemia and mild obesity.

Four-week old male ApoE*3Leiden mice were fed regular lab chow with or without a mixture of ARA (0.129 wt%) and DHA (0.088 wt%). From 12 until 20 weeks of age, mice were fed a mildly obesogenic high-fat/high-carbohydrate (HFHC) diet. Control mice received regular chow throughout the entire study. RNA was isolated from snap frozen brain tissues at 20 weeks of age and subjected to gene expression analyses using Illumina mouse microarrays and quantitative Real-Time PCR.

Pretreatment of animals with ARA/DHA can influence changes in brain gene expression evoked by HFHC feeding as shown by microarray analysis. Consistently both gene expression analysis methods demonstrated that brain TNFα gene expression was increased after HFHC diet feeding as compared to the regular chow fed group. Strikingly, this detrimental effect could be prevented by ARA/DHA intervention early in life. Besides, other genes of interest (e.g. BDNF, Caspase-3, Leptin) were significantly influenced.

This study suggests that inflammatory processes in the brain caused by an obesogenic diet later in life can be reduced by early ARA/DHA supplementation. As this central inflammatory process may also affect cognitive functioning associated with obesity, functional brain read outs consequences for behavior and potential mechanisms will be further explored.

III-10 Maternal immunization targets diabetic in utero programming in their offspring

Poster of Distinction

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Background: Approximately 20% of pregnancies are complicated by maternal diabetes. Hence, prevalences of maternal dysmetabolic conditions therefore expect to lead to a wave of diabetes and metabolic-linked diseases in their offspring. However, little is known about specific molecular mechanisms being involved in cross-generational diabetic programming and its prevention, except for diabetes-asscoiated atherogenic programming, which involves mechanisms of oxidative stress and can be targeted by antioxidants administered in prior to pregnancy. We established a novel in vivo model targeting diabetic in utero programming by maternal immunization in prior to pregnancy.

Design: Insulin resistance and type 2 diabetes were analyzed on a LDL receptor-deficient (LDL-/-) nutritive modulated mouse model as described earlier in detail. Activities of antioxidant enzymes and glutathion concentration were determined in offspring in addition.

Results: Maternal immunization improved glucose responses targeting mechanisms of oxidative stress improving diabetic, metabolic as well as cardiovascular in their offspring. Hepatic activities of antioxidant enzymes displayed clearly higher concentrations in offspring of oxLDL immunized mothers compared to age- and gender-matched controls. To exemplify, ca. 35% and 32% increase in cytosolic and total SOD (P=0.001;P=0.005), 29% increase in GPx (P=0.05) and rising 11% with respect to catalase. Mitochondrial SOD activity was significantly higher in offspring of OxLDL immunized mothers, too.

Conclusions: Maternal immunomodulation in prior to pregnancy targets diabetic, metabolic as well as cardiovascular in utero programming in their offspring. Hence, maternal oxLDL immunization alters hepatic mRNA expression and raises the activity of antioxidant enzymes in offspring targeting metabolic as well as cardiovascular programming.

III-50 Effect of Breastfeeding on Serum Osteoprotegerin in Neonates

☆ New Investigator Award Poster of Distinction

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Background: Human breast milk, the sole source of nutrition during the early neonatal period, is rich in nutrients, hormones, growth factors, and immunoactive molecules, which influence the growth, development, and immune status of the newborn infant. It had long been thought that breast milk is an adequate source of anthracitic activity for the newborns and growing child.

Objective: Human milk is a complex biologic fluid which contains nutritional and protective factors such as Osteoprotegerin (OPG), at levels 1000-fold higher than normal human serum. Since OPG and Receptor activator of nuclear factor-kappa B ligand (RANKL) system are tightly involved in bone remodeling and immune activity, the study was designated to evaluate the effect of breastfeeding on serum soluble receptor activator of nuclear factor-kappa B ligand (sRANKL) /OPG ratio in full term neonates in comparison with those of formula feeding full term neonates.

Materials and Methods: In this cross-sectional study serum levels of OPG and sRANKL in 45 breastfed infants were compared to those of 44 formula-fed full term infants. The levels of serum OPG, sRANKL, and Tumor necrosis factor alpha (TNFα) were determined by standard techniques using enzyme-linked immunosorbent assay kits.

Results: The serum levels of OPG were significantly higher ($P < 0.001$), and the concentrations of TNFα was markedly lower ($P = 0.024$) in breastfed infants than those of formula-fed infants. No marked differences were observed between the serum levels of sRANKL in the two study groups ($P = 0.8$).

Conclusions: High OPG and low TNFα levels in serum of breastfed infants are important factors involved in remodeling of bone, and immune activity may prove superiority of breastfeeding over formula feeding during infancy.

Keywords: Breast Feeding; Infant Formula; Osteoprotegerin; sRANKL; Tumor Necrosis Factor-Alpha (TNFα)

III-11 Fetal programming of the heart: decrease of cardiomyocyte proliferation in rats with intrauterine growth restriction through a loss of Wnt-/ß-Catenin signalling

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Introduction: Intrauterine growth restriction (IUGR) affects 5-10% of newborns and is associated with development of hypertension, diabetes and increased risk of cardiovascular disease in adulthood. Cardiovascular disease is of major concern worldwide. A recent clinical study detected that children with IUGR have less efficient hearts and the severity of dysfunction was strongly associated to the severity of IUGR. We hypothesize that adverse intrauterine conditions which cause IUGR affect cardiogenesis through downregulation of the Wnt /ß-Catenin - Pathway and therefore lead to primary cardiac changes which predispose for cardiac disease in later life.

Methods and Results: We studied offspring of pregnant rats treated by uterine artery ligation or sham operation on day 18 of pregnancy compared with untreated control 24 hours after intervention. Fetal hearts of offspring with IUGR show significant decreases in Wnt 2b and ß-Catenin protein expression which are essential key molecules in the process of cardiogenesis und cell proliferation. Furthermore we detected a decrease in protein expression of proliferating-cell nuclear antigen (PCNA) which is a valid marker for cell proliferation. Nkx2,5, an early marker for terminally differentiated cardiomyocytes, was, consistent with our data, also a significantly reduced gene expression (real-time PCR).

Conclusions: The findings demonstrate a decrease in cardiomyocyte proliferation through downregulation of Wnt-/ß-Catenin signalling after IUGR, which may contribute to less sufficient hearts. Since cardiomyocyte proliferation ceases soon after birth and therefore the number of cardiomyocytes is limited, this can be a high risk factor for cardiovascular disease in later life.

III-12 Intergenerational effects of a maternal high fat diet on feto-placental development in a rabbit model

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We have shown that the maternal administration of a high fat diet (H) in a rabbit model, before and during pregnancy, induces sex-dependent metabolic adaptations in the placenta from F1 generation. Here, we have focused on the consequences of this diet on the fetal biometry and placental gene expression in the F2 offspring.

Rabbit females were fed with a control diet (C) or H diet from 10 weeks of age throughout pregnancy and lactation. After weaning, the female offspring (F1) received either a C diet (groups CC and HC) or an H diet (groups CH and HH). They were mated at 18 weeks of age. At 28 days of gestation, the fetuses (F2) and their placentas were collected.

The fetal weight and the fetal to placenta-deciduas weight ratio were significantly lower in HH and CH compared to CC, whereas they increased in HC compared to CH.

Relative gene expression of lipid metabolism indicated that FATP-4 mRNA was significantly higher in HC compared to CC. SLC2A1 mRNA, a glucose transporter, was significantly increased in HH compared to the other groups, whereas SLC2A3 expression was higher in CH compared to CC, HC and HH groups. SLC38A1 and SLC38A2, which are involved in the transfer of amino acids, were significantly higher in HC compared to CC. Moreover, SLC38A2 was increased in CH compared to CC.

These data established that the grandmother's and the mother's diets interfered to disrupt nutrient exchanges in the placenta from the F2 generation.

III-13 Transcriptional responses of porcine foetuses to gestational diets varying in amounts of methylating micronutrients

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Nutritional supply of pregnant females is known to affect the progenies development. Epigenetic modifications, including DNA methylation, contribute to the phenomenon of nutritional programming. Because pigs (Sus scrofa) share many features regarding genome, physiology, and metabolism with humans, we monitored the longitudinal expression changes due to gestation diets enriched for compounds of the one-carbon-cycle in a porcine model. Pregnant Pietrain sows (n=18) were randomly assigned to receive either a standard diet without supplements (C) or a standard diet supplemented with methionine, choline, vitamin B6, vitamin B12, folic acid, and zinc (M). Foetal liver was collected at 35, 63, and 91 days post-conception (dpc; n=136). Differential gene expression of foetuses was assessed using the Affymetrix platform (n=32). Additionally, promotor methylation pattern (bisulfide sequencing), transcript abundance (qPCR), and protein yield (quantitative Western Ligand Blot) of selected transcripts were analysed. In general, a hierarchical ordering of transcriptional differences among the various subgroups appeared, such that ontogenetic stage demonstrates the largest effect followed by diet. At stage 91 dpc, both male and female M-foetuses were heavier than their age-matched controls. Consistently, different transcriptional abundances among dietary groups and ontogenetic stages culminated at 91dpc, particularly for genes related to cell cycle, tRNA charging, and proliferation. However, it remains elusive whether those transcripts are part of a primary response mediated by superior genes/processes which govern the physiological response of foetuses. The findings focus on early tissue development and reveal novel aspects regarding the relationship of the supply of methylating micronutrients, epigenetic modifications and gene expression.

III-14 Influence of maternal body composition and infant feeding on infant body composition

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Background: Maternal factors are thought to strongly influence a child's risk of obesity and metabolic dysfunction. Few studies have examined the relationship between maternal pregnancy body composition and infant body composition in the first year of life.

Objective: This prospective observational study examined the relationships between maternal body composition in the first trimester, infant feeding practices and infant body composition at four months of age.

Methods: Women were recruited at their convenience inJuly 2012 after sonographic confirmation of a singleton pregnancy in the first trimester. Maternal body composition was measured using 8-electrode bioelectrical impedance analysis. Infant body composition was measured using air displacement plethysmography at 4 months of age. Infant feeding practices were collected at 4 months of age.

Results: Of the 100 mother-infant pairs, the mean maternal BMI was 26.5 kg/m2 (± 5.7) and 22% were obese. Mean birth weight was 3.4 kg (±0.6) and infant weight at 4 months was 6.4 kg (± 0.6). The mean infant fat percentage at birth was 10.8% (1-23) and at four months was 25% (13-33). Maternal percentage fat in the first trimester was not predictive of infant % fat at four months of age. By four months of age 61.5% of mothers had introduced solids.

Conclusion: Influences on early infant growth are complex. Maternal body composition in the first trimester of pregnancy does not appear to influence infant adiposity at four months of age.

III-15 Does the 10th percentile matter in the small placenta at term: Neonatal morphometry and placental dimensions in a population based community sample

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Lifelong cardiovascular and metabolic diseases reflect adaptations to variable placental nutrient supply relative to fetal need. Small term infants are well studied, yet extensive studies haven't researched small placentas at term. At New York Methodist Hospital, with a diverse birth cohort of >5500/annum, all placentas are referred for expert pathologic review by a single observer (CMS). 157 consecutive

nonanomalous singleton livebirths with placentas < 400g at 37-41 weeks gestational age (GA) were further categorized having placental weight (PW) greater or less than (< ,>) the 10thcentile (%) by week according to published norms. Records reviewed for maternal complications, fetoplacental ratios (FPR), ponderal indices (PI), and neonatal complications (NICU admission). 87 had PW< 10th% and 70 had PW>10th%. PWs of course differed between groups. Placental chorionic plate surface area (CPA) was 15 cm2 less in PW< 10th% (p=0.026), but disk thicknesses did not differ between groups. Birthweight (BW)% differed (p=0.005), but no difference in mean BWs. FPR differed (< 10th%, 8.4+1.2 v. 7.7+0.82, p< 0.0001) although PI did not (< 10th% 2.84+0.36 v. 2.76+0.33, p=0.12). FPR and PI were positively correlated (p=0.015). Larger FPR implies, in those with PW>10th%, increased fetal size is correlated with greater nutrient demand per gram of PW, but higher FPR was also correlated with fatter newborns overall. In small placentas, fetal fat accretion is preserved at the expense of increased placental nutrient demand. A distinguishing feature of PW< 10th% is smaller CPA-which is a direct reflection of the maternal arterial number available for fetoplacental supply.

III-16 Influence of early pregnancy diet on neonatal body composition

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Background: Maternal nutritional intake mayprogramme fetal growth.

Objective: This prospective observational study examined the relationship between maternal nutritional intake in the first trimester and neonatal body composition measured directly using air displacement plethysmography.

Methods: Women were recruited in February 2013 after sonographic confirmation of a singleton pregnancy in the first trimester. Clinical and socio-demographic details were recorded and maternal body mass index (BMI) measured. Dietary information was collectedat the same visit using a validated food frequency questionnaire (FFQ). Neonatal body composition was measured within three days of delivery.

Results: Of the 75 mother-infant pairs, the mean maternal BMI was 25.1 kg/m2(± 5.7)and 14.8% were obese. The mean birth weight was 3.5 kg (±0.5) and mean percentage body fat was 10.8% (±4.5). Mean percentage energy intakes from protein, fat, and carbohydrate were 17.2 %, 35.5 %, and 49.7% respectively. There was no association between birth weight and maternal energy intakes from protein, fat, and carbohydrate. However the mean infant fat percentage for mothers in the lowest fat consumption quartile was 8.7% compared to 12.5% in the highest quartile (p=0.02). Mean infant fat percentage for mothers in the lowest carbohydrate consumption quartile was 13.1% compared to 9.1% in the highest quartile (p=0.003). Neonatal adiposity was not associated with maternal protein intake.

Conclusion: These findings suggest that interventions that decrease maternal fat intake in early pregnancy may decrease neonatal adiposity and thus, potentially, the lifelong risk of metabolic dysfunction.

III-17 Variable methylation potential reflective of imbalanced micronutrient status in preterm pregnancies

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Our earlier studies in preterm pregnancy show reduced levels of long chain polyunsaturated fatty acid (LCPUFA), altered levels of micronutrients (folate and vitamin B12) and higher homocysteine at delivery which are associated with poor birth outcome. We have demonstrated that folic acid, vitamin B12 and omega-3 fatty acids are interlinked in 1-C metabolism which is implicated in the intrauterine programming of non communicable diseases in later life. We hypothesize that alterations in micronutrients may affect the regulation of enzyme methionine adenosyl transferase (MAT) in placenta resulting in altered production of methyl donor s-adenosyl methionine (SAM). This may lead to a variation in SAM: SAH ratio resulting in altered methylation potential. The present study therefore examines the mRNA and protein levels of enzyme MAT, SAM, (s-adenosyl homocysteine) SAH levels and levels of fatty acids from preterm and term placentae. A total of 52 women each delivering preterm (< 37 weeks gestation) and delivering at term (≥37 weeks gestation) were recruited. The mRNA levels of MAT were analyzed by qRT-PCR, protein levels by ELISA, SAM-SAH levels by HPLC and fatty acid levels by GC. The SAH levels showed a significant increase (p< 0.05) whereas the SAM: SAH ratio decreased (p< 0.05) in the preterm group as compared to term. Increased SAH levels directly affect the methyl transferase reactions and this change is reflected in the lowered global DNA methylation patterns observed. The lowered methylation potential may have important implications for the epigenetic programming of the developing fetus.

III-18 Embryonic cholesterol metabolism under the influence of maternal insulin-dependent diabetes mellitus: Insights from the rabbit model

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Children exposed in utero to maternal diabetes are at higher risk for neonatal macrosomia and metabolic diseases later in life. We suppose that embryonic programming is caused to a great extent by uterine metabolites and starts as early as during the preimplantation period. Therefore we have analyzed the cholesterol metabolism as a possible target for metabolic programming in a diabetic pregnancy model of the rabbit.

Cholesterol concentration was measured by fast protein liquid chromatography (FPLC) analysis in blood serum and uterine fluid of pregnant females at day 6 post coitum. In diabetic rabbits the cholesterol levels were increased and accompanied by changes in the lipoprotein composition of VLDL, LDL and HDL. The mRNA expression of HMGCR, LDLR, VLDLR, SREBP-2, INSIG-1 and CYP7A1 was altered in hepatic and adipose tissue.

Preimplantation rabbit embryos expressed HMGCR, LDLR and SREBP-2 from day 3 p.c. onwards, whereas VLDLR and INSIG-1 were first present at the blastocyst stage. In blastocysts from diabetic rabbits moderate alterations in gene expression related to cholesterol

metabolism were observed with an increased SREBP-2-to-INSIG-1 ratio and an increase in LDLR mRNA expression. In vitro experiments revealed glucose - but not insulin-dependent HMGCR expression in blastocysts.
We conclude that maternal diabetes leads to increased cholesterol levels in the uterus during periimplantation period. The maternal hypercholesterolaemia is not mirrored in comparable strong alterations in embryonic metabolism.
This work was supported by the EU (FP-7 EpiHealth No 278418) and the Wilhelm Roux Programme of the MLU Faculty of Medicine.

III-19 Maternal hypoxia elicits a maternal stress response, impairs fetal growth and alters the placental glucocorticoid regulatory system in mice

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Maternal hypoxia is a common perturbation that both reduces oxygen uptake and elicits a maternal stress response. Fetal exposure to either reduced oxygen levels or glucocorticoids (cortisol in humans and corticosterone in rodents) is capable of impairing organ formation and programming offspring disease. The placenta is known to regulate fetal exposure to oxygen, nutrients and glucocorticoids but its role in maternal hypoxia induced programming of disease is unknown. This study aimed to investigate the placental adaptations to maternal hypoxia that may regulate/contribute towards fetal outcomes. CD1 mice were housed under 21% or 12% oxygen from embryonic day (E) 14.5 until tissue collection at E18.5. Maternal corticosterone was measured and placentas were sexed and collected for the analysis of gene and protein expression. Maternal hypoxia increased maternal corticosterone by 40% and reduced fetal weight by 7%. While hypoxia did not directly affect placental weight, placentas of female fetuses of hypoxic dams had increased labyrinth vascular branching. Maternal hypoxia reduced placental mRNA expression of the mineralocorticoid and glucocorticoid receptors and reduced the gene and protein expression of the glucocorticoid metabolizing enzyme, HSD11B2 and GLUT1. In summary, maternal hypoxia elicited a maternal stress response which may have contributed to reduced fetal growth and altered placental formation. Additionally, maternal hypoxia alters the expression of factors involved in placental glucocorticoid signaling and the regulation of fetal glucocorticoid exposure.

III-20 Establishing an animal model of passive exposure to tobacco smoke during pregnancy

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Many studies have linked maternal smoking during pregnancy with increased risk for adverse outcomes in newborns, such as intrauterine growth restriction and low birth weight. In this work, we proposed an animal model of tobacco passive exposure during gestation to investigate its effects on fetal growth and biochemical parameters, using cotinine and carboxyhemoglobin as exposure markers. Exposure - pregnant rats were randomly assigned to the groups: control, manipulated control and tobacco (exposed to a one cigarette twice a day for 21 days of gestation). The manipulated control group went through the same intervention of tobacco group, without suffering smoke exposure; control group remained intact in the home cage. On 22nd day of pregnancy pups were surgically delivered. Immediately after, maternal trunk blood was collected for markers and biochemical measurements. Trunk blood of the pups was also collected and fetal biometry measured. The proposed experimental model of tobacco exposure during pregnancy was successful in inducing high levels of carboxyhemoglobin, showing an approximate increase of 1.5% in the tobacco group when compared with the manipulated control group ($P < 0.0001$). We found a mean cotinine value of 42.5 ng/mL in the exposed animals, whereas the control and manipulated control groups had undetectable values. In addition, tobacco exposure during the intrauterine period significantly decreased the birth weight ($P = 0.005$), serum glucose ($P < 0.0001$) and insulin ($P < 0.009$) of the pups. The model was able to mimic alterations observed in human newborns whose mothers were exposed to tobacco during gestation.

III-21 Is high fat diet-induced hypothalamic plasticity modified by intrauterine growth restriction?

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Introduction of a high fat diet has recently been found to modify the anorexigenic tone by reducing the number of excitatory synapses onto orexigenic primary neurons and by reducing inhibitory synapses onto anorexigenic neurons in the arcuate nucleus of rats resistant to diet-induced obesity. We previously showed that intrauterine growth restriction altered brain development and reduced the number of arcuate nucleus fibers containing NPY and POMC peptide that projected to the PVN. These features could be at the origin of leptin resistance and diet-induced obesity.
Therefore we investigated arcuate nucleus plasticity in response to high fat diet in a model of IUGR. Sprague-Dawley rats were fed chow either ad libitum (100%, n=18) or 50% of that amount (n=16) throughout pregnancy. All mothers continued on chow ad libitum until weaning. Male offspring either stayed on chow throughout (100% chow, n=34; 50% chow, n=33) or were changed to a high fat diet (100% HFD, n=52; 50% HFD, n=50) on 28 days postnatal. Hypothalami were examined by the evaluation of pre- and postsynaptic markers at 29, 33, 36 and 120 days of age.
Maternal nutrient restriction led to a lower birth weight (84% of non-restricted). Introducing a high fat diet induced a significant short-term increase in food intake (200% of chow caloric intake on the first day of introduction) and a moderately higher intake (130% and decreasing) after three weeks on this diet, demonstrating an adaptation to the diet. Body fat mass, glucose tolerance and synaptic plasticity will be presented.

III-22 Maternal corticosterone exposure in the mouse alters the mineralocorticoid system in the fetus and adult offspring

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Maternal exposure to synthetic glucocorticoids (GC) during pregnancy is known to impair fetal kidney development and program poor health outcomes in offspring. Less is known about how maternal exposure to endogenous GC (corticosterone in rodents) can alter renal

development and physiology. While synthetic GC bind to the glucocorticoid receptor (GR) to elicit their biological effects, natural GC act on both the (GR) and the mineralocorticoid receptor (MR). This study aimed to identify the effects of maternal corticosterone exposure on fetal and offspring renal MR and GR expression in male and female fetuses. Pregnant C57/BL/6 mice were either left untreated or surgically implanted with osmotic minipumps primed to release Corticosterone (33µg/kg/h, 60h beginning at E12.5). At E14.5, dams were killed and kidneys collected for qPCR analysis of MR and GR expression. Additional mice littered down with offspring kidneys and plasma collected at 6 months of age for analysis of plasma aldosterone levels and renal MR and GR mRNA. Maternal corticosterone exposure increased renal mRNA levels of MR and GR in male but not female E14.5 fetuses. At 6 months of life, maternal corticosterone exposure increased plasma aldosterone levels and increased MR and GR mRNA levels in kidneys of males only. This study demonstrates that prenatal corticosterone exposure can directly affect not only the glucocorticoid signaling pathway but also the mineralocorticoid system. This may contribute to the programmed alterations in renal function and blood pressure commonly seen in the male offspring of dams exposed to perturbations that may affect maternal stress.

III-23 Comparison between neonatal body composition at birth and maternal smoking status in the first trimester

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Aim: This study examined the relationship between neonatal body composition and maternal smoking status in the first trimester.
Methods: Women were recruited in the first trimester of pregnancy following ultrasound confirmation of a viable singleton pregnancy and accurate assessment of gestational age. Maternal current smoking status was recorded and maternal body composition was measured by 8-electrode bioelectrical impedance analysis. Babies born before 37 weeks gestation were excluded. Neonatal body composition was measured within three days of birth by air displacement plethysmography.
Results: Of the 257 mothers recruited, 15% (39/257) were current smokers. The mean maternal age was 27.5 years in the smokers and 31.0 years in non-smokers (p=0.009). There were no differences in maternal body composition between the two groups; 18% of smokers were obese and 20% of non-smokers (p=0.7), the mean BMI in smokers was 25.9 kg/m2 and 26.2 kg/m2 in non-smokers (p=0.8), the mean maternal percentage body fat was 30.7% in smokers compared to 32.8% in non-smokers (p=0.4). The mean birthweight was lower in babies born to mothers who smoked; 3.23 kg compared to 3.5kg in non-smokers ($p < 0.05$). Infants born to smoking mothers had a trend towards a lower percentage of body fat with a mean of 9.7% compared to 15.2% in infants born to non-smoking mothers (p=0.1).
Conclusion: Babies born to smoking mothers are smaller and have less body fat. They are therefore more likely to have an accelerated growth trajectory in early infancy with the resulting potential for life-long metabolic abnormalities.

III-24 The relationship between gestational weight gain and neonatal body composition

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Aim: This study examined the relationship between gestational weight gain and neonatal body composition.
Methods: Women were recruited in the first trimester of pregnancy following ultrasound confirmation of a viable singleton pregnancy and accurate assessment of gestational age. Maternal body composition was measured by 8-electrode bioelectrical impedance analysis in the first trimester and again after 37 weeks gestation and gestational weight gain was calculated. Pregnancies not reaching 37 weeks gestation were not included in the analysis. Neonatal body composition was measured within three days of birth by air displacement plethysmography.
Results: There were 91 mother-infant pairs included in the analysis. The mean maternal BMI was 26 kg/m2 and 16% were obese. The mean infant birth weight was 3.48kg (±0.48) and the mean infant percentage fat was 10.9 % (± 3.9). The mean gestational weight gain was 11.6 kg (±4.9). Gestational weight gain did not correlate with birth weight (p=0.17) or infant fat mass (p=0.29) or infant percentage fat (p=0.46).
Conclusion: Factors influencing fetal growth are complex and gestational weight gain does not appear to influence infant birth weight or fat composition.

III-25 Fatty acid desaturase single nucleotide polymorphisms and plasma concentrations of arachidonic and docosahexaenoic acids in Mexican pregnant women

EARLYNUTRITIONMEMBER

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An adequate supply of polyunsaturated fatty acids (PUFAs), particularly arachidonic acid (AA) and docosahexahenoic acid (DHA), is important for fetal brain growth and development. Specific single nucleotide polymorphisms (SNPs) in the fatty acid desaturase genes (FADS) modulate AA and DHA status. We examined associations between 15 FAD SNPs and pre-supplementation plasma concentrations of AA and DHA in 136 pregnant women who participated in POSGRAD, a randomized controlled trial of supplemental DHA on infant growth and development in Cuernavaca, Mexico. Mean (±SD) plasma concentration of AA and DHA were 7.2 ± 1.6 and 2.3 ± 0.6 mg/dl respectively. Using linkage disequilibrium maps, we selected 4 tag SNPs (rs174445, rs174556, rs174602, rs498793) that accounted for

most of the variability in PUFA plasma levels (r2 between 0.05 and 0.47). After Bonferroni correction for multiple comparisons, rs174556 was positively associated with plasma concentration of both AA (0.78±0.02, p< 0.001) and DHA (0.1±0.04, p=0.003); whereas, rs174445 was associated only with plasma DHA (0.1±0.04, p=0.009). These results are consistent with other evidence linking these SNPs to human plasma PUFA concentrations. In future work we will use these data to determine if there are selective impacts by FADs SNPs of prenatal DHA supplementation on offspring growth and development.

III-26 The relationship between infant birth weight and maternal lipid levels in the third trimester of pregnancy

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Aim: The purpose of this study was to examine the relationship between maternal lipid levels and infant birth weight in women selectively screened for gestational diabetes mellitus (GDM).

Methods: Women undergoing an oral glucose tolerance test for GDM screening early in the third trimester of pregnancy had a fasting lipid profile performed. Clinical and socio-economic data were recorded and infant birth weight was measured immediately after delivery.

Results: Of the 189 women recruited to the study, the mean age was 32 years and 35.4% were primigravid, 44.1% were obese and 11.6% were diagnosed with gestational diabetes mellitus. Increasing birth weight was associated with multiparity, first trimester body mass index, gestational diabetes mellitus and hypertriglyceridaemia on univariate analysis. On multivariate analysis increasing birth weight correlated positively only with hypertriglyceridaemia. For birthweights less than 3.00 kg, 3.00-3.49kg, 3.50-3.99kg and greater than 4.00 kg the respective mean maternal fasting triglyceride levels were 1.58, 1.88, 1.87 and 2.23 mmol/L.

Conclusion: Fetal growth is influenced by maternal circulating triglyceride levels. This raises the question as to whether women of childbearing age should be screened for hypertriglyceridaemia.

III-27 Fetal plasma LpPLA2 activity is altered by hyperglycemia during pregnancy

EARLYNUTRITIONMEMBER

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Objectives: Lipoprotein associated phospholipase A2 (LpPLA2) detoxifies oxidized phospholipid species. In adults, LpPLA2 is produced by macrophages and carried by lipoproteins (80% LDL, 20% HDL). Some studies suggest that association of LpPLA2 with lipoprotein particles determines its pro- or anti-inflammatory properties. In pathological conditions, e.g. diabetes, total serum LpPLA2 activity was shown to be increased.

The aim of this study was to describe origin and functionality of LpPLA2 in fetal circulation and to answer whether pathological conditions during pregnancy (gestational diabetes [GDM] and obesity) may alter LpPLA2 activity.

Methods: LDL and HDL were isolated from control and GDM cord blood plasmas (n=6). Primary fetal placental macrophages (HBCs) were exposed to hyperglycemia (25mM glucose). LpPLA2 activity was measured on fetal lipoproteins and in supernatants from HBC cultures. LpPLA2 mass was analyzed in cell lysates.

Results: In contrast to adults, LpPLA2 activity was higher on fetal HDL than on LDL particles (p< 0.001). GDM increased total fetal plasma LpPLA2 activity (p< 0.001, ~70%). HBCs were shown to express LpPLA2, unlike placental endothelial and trophoblast cells. Glucose treatment decreased LpPLA2 protein production from macrophages (~35%; p=0.003), specific LpPLA2 activity was increased (~66%).

Conclusions: Our results show that in fetal circulation LpPLA2 is mainly associated with HDL particles. GDM alters LpPLA2 activity, both on fetal HDL and LDL particles. Placental macrophages express LpPLA2; their reaction to hyperglycemia reflects the increase in LpPLA2 activity found in GDM plasma. Unique distribution of LpPLA2 in fetal circulation may exert its anti-inflammatory functions and represent a protective mechanism.

III-28 The relationship between infant birthweight and neonatal body composition

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Birth weight has been used as a marker of adiposity in neonates. Newer techniques provide safe, accurate measurements of the body fat of newborn infants. This study describes relationship between birth weight and neonatal body composition.

Infant body composition was measured within three days of delivery using air displacement plethysmography (PEAPOD, COSMED, Rome Italy). Term infants born between 37-42 weeks gestation were included in the analysis.

Measurements were performed on 352 infants. The mean birth weight and gestational age were 3.48kg and 39.6 weeks respectively. The mean percentage fat increased as birth weight quartile increased. The mean fat percentage for the lowest, second, third and highest birth weight quartiles was 7.3%, 8.6%, 11.8% and 13.2% respectively. However the range of body fat percentages measured did not vary between the quartiles.

Babies in the lowest birth weight quartile have a similar range of percentage body fat to babies in the highest birth weight quartile. Infant birth weight is not an accurate marker of infant adiposity. Studies exploring influences on neonatal adiposity must be based on direct measurement of infant fat and not on birth weight.

III-29 Effects of neonatal dexamethasone exposure on metabolic imbalance and oxidative stress marker in the liver of male albino rats

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It has been reported in human and animal studies that early exposure to glucocorticoids could retard growth and subsequent develop-

ment of cardio metabolic diseases. The role of oxidative stress in some of the metabolic imbalance needs to be elucidated. This study examined the effects of neonatal dexamethasone exposure on metabolic imbalance and oxidative stress marker in the liver of offspring of exposed mother.
The rats were divided into 4 groups. Group 1 was administered 0.02ml/100gbwt/day normal saline through postnatal (PN) day 1-21. Group 2,3, and 4 were administered 100µg/kg bwt / day dexamethasone (Dex) for PN day 1-7,1-14, and 1-21 respectively. All administration were done subcutaneously. The male offspring were separated, monitored and sacrificed at 12weeks of age for evaluation of lipid profile and oxidative stress in the liver.
Total Cholesterol (TC), Triglyceride (TAG) and LDL were significantly higher in the treatment groups when compared with the control.HDL was significantly reduced in all the treated group relative to the control. Basal Fasting blood sugar (FBS) was also significantly higher in the Dex1-14, Dex 1-21 groups when compared with the control and Dex 1-7 group. Liver malondialdehyde was significantly higher in the Dex1-14, and Dex 1-21 group compare to the control and Dex1-7 group. However, liver catalase, SOD , protein and total plasma protein level were all significantly lower than the control.
Results suggest that increase occurrence of metabolic diseases in offspring of mother that have been exposed to dexamethasone may be due to increase in the oxidative stress in the liver.

III-30 Exposure to a high-caloric diet in utero reduces metabolic flexibility in the liver in rat offspring when fed a high-fat diet during adulthood

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Perinatal exposure to energy-dense diets increases the risk for metabolic diseases in the offspring. This might be due to reduced metabolic flexibility, i.e. a reduced capacity to adapt to altered metabolic requirements.
To study this, rat dams were given a high fat/high sucrose diet (H) or a chow-diet (C) 6 weeks prior to mating as well as during gestation and lactation. Pups were cross-fostered the day after birth, giving rise to four groups defined by dietary exposure (C or H) during pre- and post-natal life. The offspring were weaned onto a chow diet and challenged with a high-fat diet (45 E%) from 20-26 weeks of age. Tissues were collected after the challenge, and hepatic lipid composition and gene-expression for genes in the related metabolic pathways were analysed.
The high fat diet caused increased hepatic triacylglycerol accumulation in all groups, regardless of maternal diet. However, offspring born by high caloric dams had significantly increased FFA levels (effect of prenatal diet $p< 0.0001$), lactation by high-caloric fed dams further increased this effect. Median hepatic FFA level was 4.3 fold higher in these animals compared to rats born by C-fed dams but lactated by H-fed dams ($p< 0.0001$). Based on fatty acid composition, we show that this effect is due to hampered metabolism of dietary polyunsaturated fatty acids.
In conclusion, pre-natal exposure to high-caloric diets reduced the hepatic capacity of shunt hepatic FFA into the appropriate pathways and might hence induce lipotoxic effects in the liver after high-fat intake.

III-31 Changes in ovine adipose tissue in early postnatal life

EARLYNUTRITIONMEMBER

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Background: Adipose tissue appearance and composition changes rapidly in early life. Brown adipose tissue (BAT) is present in newborns and is subsequently replaced by white adipose tissue (WAT). In perirenal adipose tissue, the largest BAT depot in newborn sheep, BAT gradually disappears in the postnatal period to be replaced by WAT by 30 days of age. We have studied the changes in adipose tissue appearance and presence of uncoupling protein (UCP)1, unique to BAT protein, in epicardial, pericardial and subcutaneous fat depots of postnatal sheep.
Methods: Changes in adipose tissue composition were investigated by immunohistochemistry of samples taken from epicardial, pericardial and subcutaneous depot of sheep (n=5-10) at 1, 7 and 28 days of life. Each sample was fixed in formalin and embedded in paraffin and 5µm sections stained and analyzed using Volocity software and the relative abundance of UCP1 quantified.
Results: There was a high abundance of UCP1 positive, multilocular adipocytes in paracardial and epicardial, but not subcutaneous, depots on day 1 that gradual disappeared by day 28 in all three depots.
Conclusion: Both epicardial and paracardial fat, the two components of pericardial adipose tissue, are BAT depots in the newborn whilst the subcutaneous depot has a mixture of BAT and WAT. All three depots undergo a gradual transition with disappearance of UCP1 expressing brown adipocytes and that are replaced by large, unilocular, lipid filled cells.

III-32 Novel in silico model characterizes metabolic programming using the Protein-Kinase B-alpha (PKBα-/-) in vivo model

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Introduction: Since the variety of parental risk factors is associated with a wide spectrum of metabolic outcomes in their offspring it is highly recommended to characterize metabolic constitutions in prior to pregnancy first and precisely. Therefore, we established a specific in silico assessment tool targeting metabolic characterizations individually.
Materials and methods: Body weights, fasting blood glucoses, insulin concentrations, oral glucose tolerance tests (OGTT) and intraperitoneal insulin tolerance test (IPITT) were performed on Protein-Kinase B-alpha (PKBα-/-; KO) mice as well as the gender- and age-matched control groups (WT). The pathophysiological state of metabolic programming, e.g. due to determining the specific grade of insulin sensitivity (IS) was analyzed by applying the established in silico model. Hence, the individual course of metabolic progress could be exactly

predicted additionally.
Results: Although, KO mice do suffer from equal gene defects, each mouse displayed a different metabolic profile. But, generally speaking, male PKB-/- mice (KO) presented significantly increased IS at an age of 6 months, whereas age-matched male control group (WT) developed clear features of an insulin resistance (IR) ($p \leq 0.05$). Commonly, female groups (KO and WT) displayed improved glucose sensitivities compared to age-matched males (KO and WT) manifested in superior glucose tolerances, for example (for WT $p \leq 0.011$).
Discussion: Specific metabolic characterization should be assessed individually. Therefore, our in silico model enables novel insights targeting metabolic profiles in prior to pregnancy specifically. Hence, specific primary preventive strategies targeting cross-generational metabolic programming in their offspring may be conceivable.

III-33 Modulation of autophagy in the liver of offspring of animals treated with high fat diet during intrauterine life and lactation

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Autophagy is an important lisossomal degradation mechanism that maintains the cellular homeostasis by eliminating malformed proteins, damaged organelles, pathogens and intracellular recycle nutrients, thus contributing to cellular energy homeostasis. Recent studies have suggested that autophagy may be compromised in metabolic diseases situations as obesity. Evidences suggest that early life environment can result in epigenetic changes and lead to profound and prolonged effects on long term health of the offspring. Here we evaluated whether diet-induced obesity during pregnant and lactation periods could induce autophagic defect in the liver of the offspring in early life. We used swiss female mice fed with control or high-fat diet during this two periods and evaluated autophagic markers in the liver of offspring (PC and PH respectively) on the day of birth (D0) and after lactation (D18). Although no difference in body weight was found in D0, we observed decreased gene expression and protein content of LC3 II and increased gene expression of p62 in PH when compared to PC. Interestingly after weaning (D18) we observed an increase in body mass, retroperitoneal and epididymal fat. Also, the animals exhibited decrease protein content of LC3 II and increased gene expression of p62 in the liver of PH, which are important markers of the autophagy pathway. We conclude that high-fat diet during pregnancy and lactation could compromise autophagy activation in liver in early life of offspring, demonstrating the importance of intrauterine environment during development.

III-34 Impact of maternal and fetal inflammatory pathways on neonatal and infant adiposity

EARLYNUTRITIONMEMBER

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Aim: Maternal BMI is known to affect birth weight, and obesity is a known inflammatory condition. This study aimed to determine the impact of maternal and fetal inflammatory markers on infant anthropometry.
Methods: 265 mother-infant pairs from the ROLO study[1] were analysed. Interleukin 6 and TNF-alpha were measured in early and late pregnancy and in cord blood. Birth weight and anthropometric measurements were recorded at birth and 6 months. Various skinfolds were also measured. The sum of Subscapular + Triceps skinfolds and the ratio were used as a marker of general and central adiposity respectively[2] .
Results: IL-6 in fetal blood was found on simple linear regression to influence birth length while late pregnancy IL-6 influenced the Triceps skinfolds at 6 months of age. It had no influence over general or central adiposity.
TNFα in early pregnancy significantly influenced both general adiposity and subscapular, biceps and triceps skinfolds. Central adiposity at birth was not influenced. Central adiposity at 6m however was. Early, late and fetal TNFα were also found to correlate with various other markers of 6 month anthropometry including triceps, biceps and subscapular.
Conclusion: Maternal inflammatory markers have significant influence over neonatal and infant anthropometry. Fetal IL-6 and early pregnancy TNFα effect neonatal anthropometry, while late pregnancy IL-6 and TNFα throughout pregnancy effect 6 month anthropometry. This data emphasises the importance of the antenatal inflammatory markers in the prediction of neonatal and infant anthropometry. Their influence therefore may play a role in the predisposition towards early childhood obesity.

III-35 Gestation reverses obesity-induced adipose tissue inflammation in mice

EARLYNUTRITIONMEMBER

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Background: Maternal obesity is associated with increased risk of metabolic dysfunction in the offspring. It is not clear which physiological aspects of the obese state cause this metabolic programming. Obesity causes many metabolic changes but also chronic low-grade inflammation. Therefore, we investigated if low-grade inflammation was present in obese dams compared to controls dams at gestation day 18.
Methods: Female mice were either fed a standard chow diet or a highly palatable obesogenic diet. After 6 weeks on the diets, half the mice (n=12) were sacrificed and the remaining half were mated and sacrificed on gestation day 18 (n=8).
Results: Obesogenic diet increased body weight and decreased insulin sensitivity prior gestation, while there was no difference between the groups at gestation day 18. Local inflammation was assayed by macrophage count in adipose tissue and liver. Macrophage count in the adipose tissue was increased by the obesogenic diet, and the hepatic count also showed a tendency to increased macrophage infiltration prior gestation. This was further supported by a decreased population of monocytes in the blood of the obese animals, which could indicate that the monocytes are being recruited from the blood to the liver and adipose tissue in the obese animals. Gestation reversed the infiltration, obese dams showed lower macrophage count in the adipose tissue at the end of gestation compared to pre-gestating obese mice and there were neither any difference in hepatic macrophage count between the two dietary treatments.
Conclusion: Gestation attenuates the obesity-induced tissue inflammation in mice.

III-36 Maternal and fetal predictors of birth weight and neonatal adiposity

EARLYNUTRITIONMEMBER

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Aim: Antenatal factors predicting neonatal adiposity have yet to be fully elucidated. The aim of this study was to determine maternal, paternal and antenatal factors that influence birth weight and adiposity.

Methods: Neonatal anthropometric and skinfold measurements were recorded as markers of adiposity in 265 cases from the ROLO study[1]. In addition to maternal and paternal demographic factors, the following factors were examined in early and late pregnancy and in cord blood; Glucose, Leptin, Insulin, HOMA and C Peptide. Linear and multiple regression analysis was then performed.

Results: On linear regression birthweight was influenced by fetal leptin, gestational age, gender, maternal weight, height, BMI and paternal weight.

Overall neonatal adiposity was assessed by the sum of the subscapular and triceps skinfolds and the following were significant on linear regression: leptin at all time-points, early and late pregnancy insulin and HOMA and also fetal C-Peptide.

Central adiposity was assessed by the subscapular to triceps ratio and on linear regression only maternal fasting insulin at 28 weeks gestation was significant.

Conclusion: Birthweight was influenced mainly by maternal and paternal anthropometric factors while central adiposity [SS/TR] was solely influenced by maternal late pregnancy insulin levels in our cohort. Total neonatal adiposity [SS+TR] however was influenced by various factors in the metabolic milieu at all time-points throughout pregnancy with Leptin exerting the predominant influence.. This data emphasises the importance of the maternal and fetal metabolic status in the prediction of neonatal adiposity and subsequently in the predisposition towards early childhood obesity.

III-37 Novel in vivo model enables insights of recent consequences due to diabetic in utero programming

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Background: Approximately 20% of pregnancies are complicated by maternal diabetes. However, maternal diabetes seems to be one of the strongest risk factor "programming" diabetes in utero causing insulin resistance (IR) and type 2 diabetes (T2D) in their offspring postnatal. But, cross-generational diabetic in utero programming is still poorly understood. Therefore, we established a novel mouse model suitable to analyze mechanisms of cross-generational diabetic programming.

Design: Gestational Weight Gain (GWG) and blood glucose (BG) concentrations were determined in diabetic mothers (DM) as well as age-matched non-diabetic mothers (NDM) using an Ins2+/- mouse model respectively age- matched control groups. Offspring of DM as well as NDM were observed as described earlier.

Results: Blood glucose levels of DM were clearly higher compared to NDM during pregnancy ($p = 0.0711$). However, DM displayed a significant lower GWG compared to NDM ($p = 0.0377$). Offspring of Diabetic Mothers (ODM) did not display features of diabetic programming during suckling, but altered glucose homeostasis could be determined after weaning significantly, for example at an age of 11 weeks analyzed by an oral glucose tolerance test (OGTT).

Conclusions: Recapitulatory, our mouse model is suitable analyzing features and mechanisms of diabetic in utero programming. Beyond that, our data displayed clearly that features of IR respectively T2D are cross-generational linked due to in utero imprinting. Hence, mechanisms being involved in cross-generational diabetic programming will be addressed in the future precisely.

III-38 In a mouse model dietary methyl supplementation during pregnancy permanently alters total DNA methylation and gene expression in the hypothalamus of the offspring

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Question: Does a methyl enriched diet during pregnancy permanently modify the epigenome of the offspring in different organs?

Material and Methods: Female mice (C57BL/ 6) were fed with a methyl donator enriched diet during pregnancy. Pregnant female mice that received normal food served as controls. Offspring was killed at the age of 3 months and DNA of heart, liver, spleen, brain and hypothalamus was isolated. Total DNA methylation was determined in each organ. In addition, the hypothalamic tissue gene expression patterns between active treatment and control were compared using Differential Tissue Microarray Analysis.

Results: The total DNA methylation level of the investigated organs is listed below (control - diet): heart: 57% - 70%, liver 41% - 50%, spleen: 52% - 68%, brain 47% - 91%, hypothalamus: 6% - 26%. The gene expression patterns in the hypothalamus showed 300-fold higher expression of the Xist and a 4-fold higher expression of the folic acid receptore gene in the treatmentgroup compared to the controls.

Conclusion: A methyl donator enriched rich diet during pregnancy results in a higher total DNA-methylation in all selected organs. This effect is particularly pronounced in the brain and in the hypothalamus and leads to an increased expression of the Xist and the folic acidreceptor gene.

III-39 Maternal stress during pregnancy programs nephron deficits, gender specific hypertension and male cardio-renal dysfunction in second generation offspring

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Being born small increases cardiovascular disease risk which is not limited to the first generation (F1), but is transmitted to the next generation (F2). We characterised cardio-renal function in F2 offspring born to normally grown and growth restricted (F1) mothers and

assessed the impact of maternal stress during pregnancy.
Uteroplacental insufficiency (Restricted) or sham (Control) surgery was performed in the late gestation rat (F0). F1 females were mated and allocated to Unstressed or late pregnancy Stressed (24h metabolic cage, tail-cuff blood pressure, glucose tolerance test) groups. F2 offspring born to mothers exposed to maternal stress had reduced weight at birth but no differences thereafter. Nephron number was reduced in offspring exposed to maternal stress with males more affected. Restricted Unstressed males had higher blood pressure (6, 12 months) compared to Control Unstressed. Control stressed male offspring had elevated blood pressure (6, 9, 12 months) compared to Control Unstressed; blood pressure was similar to those born to Unstressed mothers who were born small. Maternal stress, regardless of birth weight, programmed decreased left ventricular fractional area change (echocardiography systolic dysfunction), increased relative left ventricle wall thickness and enhanced pulse pressure response to restraint stress (telemetry) in males (16months). Control, but not Restricted, Stressed males (16months) had increased albumin excretion and left ventricular hypertrophy.
Maternal stress during pregnancy regardless of maternal birth weight programmed profound cardio-renal dysfunction in the next generation; the response was exacerbated if the mother was born of normal weight and was relatively protected if she was born small.

III-40 The effects of neonatal dexamethasone exposure on some kidney function in male offspring

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It has been reported in human and animal studies that early exposure to glucocorticoids could retard growth and subsequent development of hypertension. The role of the kidney in the long term control of blood pressure has been reported in literature. This study examined the effects of neonatal dexamethasone exposure on kidney function, oxidative stress marker in the kidney and kidney architecture of offspring of exposed mother.
The rats were divided into 4 groups. Group 1 was administered 0.02ml/100gbwt/day normal saline through postnatal (PN) day 1-21. Group 2,3, and 4 were administered 100µg/kg bwt / day dexametasone for PN day 1-7,1-14, and 1-21 respectively. Administration was done subcutaneously. The male offspring were separated, monitored and sacrificed at 12weeks of age for evaluation of serum analyte, oxidative stress marker in the kidney and kidney histology.
Serum creatinine and Urea levels were significantly higher in the treatment groups when compared with the control. However, serum urea level was significantly higher in the Dex 1-7 group than Dex 1-14 and Dex 1-21. Kidney malondialdehyde was also significantly higher in the treatment groups. However, kidney catalase, SOD and plasma protein level in the treatment group were all significantly lower than the control. Meanwhile, Kidney protein was significantly lower in the control when compared with the treatment groups. Histology of the kidney showed mild, moderate and severe tubular necrosis in the Dex1-7, Dex 1-14, Dex 1-21 group respectively.
Results suggest that exposure to dexamethasone during early developmental stage could lead to damage to the kidney architecture and function.

III-41 Maternal exposure to diesel engine exhaust during pregnancy affects fetal and placental growth: validation of a rabbit model

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Maternal exposure to airborne pollution, in humans, has been shown to induce an intra uterine growth retardation associated towith a decreased placental weight. Human studies, however, are limited to investigate underlying mechanisms. Here we developed a rabbit model to study these potential effects during pregnancy.
Female rabbits were exposed to a representative air pollution mixture, i.e. diluted diesel engine exhaust (N=7, group P) or clean air (N=5, group C), 1h every morning and afternoon, 5 days a week, from 3 to 27dpc (term=31d). At 28dpc, dams were euthanized, fetuses and placentas were collected, measured and weighed. Data were analysed by ANOVA, including litter size, sex and dam as cofactors.
Altogether, 68P and 41C feto-placental units were collected. P fetuses were significantly lighter ($p < 0.001$) than C fetuses. Fetal to placental weight ratio was significantly lower in exposed compared to unexposed fetuses, indicating reduced placental efficiency. In contrast, placental and deciduas weights were not affected. Exposure was associated with reduced crown-rump length, abdominal perimeter, head length and biparietal diameter ($p < 0.05$, $p < 0.001$, $p < 0.001$ and $p < 0.05$, respectively). Brain and liver to fetal weight ratios were increased in P fetuses ($p < 0.05$), whereas lung, heart and kidney to fetal weight ratios remained unchanged, indicating that brain and liver were preserved in the P fetuses, as described in humans with disharmonious growth retardation.
These data indicate that repeated exposure to airborne pollution even for daily short periods affects fetoplacental development and validate the use of the rabbit model for further studies.

III-42 Higher Alu methylation level in catch up growth in twenty-year-old Thai offsprings

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Alu elements are human abundant intersperse repetitive sequences. Lower Alu methylation has been observed in blood cells of people with old age and in menopausal women having lower bone mass and osteoporosis. Nevertheless, Alu methylation levels also vary among young individuals. Here, we explored phenotypes that are associated with Alu methylation levels in young people. In 2010, 249 adolescents whose mothers had participated in a study association between birth weight (BW) and nutrition during pregnancy in 1990, were invited in our present study. In this study, the long interspersed element-1 (LINE-1 or L1) and Alu methylation levels and patterns

were measured in peripheral mononuclear cells and correlated with various nutritional parameters during intrauterine and postnatal period of offsprings. This included the amount of maternal intake during pregnancy, mother weight gain during pregnancy, birth weight, birth length, the rate of weight gain in the first year of life. Catch up growth (CUG) was defined when weight during the first year was >0.67 of the standard score, according to WHO data. No association with LINE-1 methylation was identified. The mean level of total Alu methylation in the CUG group was significantly higher than those non CUG (39.61% and 33.66 % respectively, P < 0.0001). The positive correlation between history of CUG in the first year and higher Alu methylation indicates the role of Alu methylation in not only in aging cells but also human growth process.

III-43 Inhibition of adiposity process by flavonoids

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Introduction: Adiposity play major role in pathogenesis of various metabolic disease, such as diabetes and cardiovascular disease that have inflammatory base. Regarding to the fat tissue commonly as an inflammatory tissue promote insulin resistance and disturb normal macronutrient metabolism, the aim of this article is mechanistic surveying the dietary flavonoids on regulation of inflammatory pathways and macronutrients metabolism in fatty tissue and ultimately controlling adiposity.

Survey Method: This article is a review on articles published in googlescolar since 2000 about the effects of falvoniods on adiposity.

Results: experimental studies indicated gene expression of peroxisome proliferator-activated receptor-γ(PPAR-γ) which affects energy substrate metabolism, glucose uptake, fat oxidation, differentiation of adipocyte and insulin sensitivity can modulate by flavonoids. The gene expression pattern of inflammatory mediators in adipose tissue upregulated, numerous flavonoids potentially can alter and suppress many inflammatory signaling pathways by anti-inflammatory roles. Flavonoids attenuate and downregulate the gene expression of tumor necrosis factor-α(TNF-α), interlekin-6 and monocyte chemoattractant protein-1(MCP-1). Possible mechanisms underlying anti-inflammatory effects of flavonoids are generally interaction and downregulation of the nuclear factor-kappa B(NF-kB) pathway and dispensably on inflammatory mitogen activated protein kinase(MAPK) pathway and then can inhibit the JNK phosphorylation and suppress the production of inflammatory mediators.

Conclusion: dietary component such as flavonoids have beneficial effects in metabolism regulation and also inflammatory processes that lead to reduction in adpogenesis, fat accumulation and insulin resistance. These food-derived, natural bioactive agents can applied as safe supplements in clinical trial studies for surveying its efficacy in human.

III-44 Investigating tryptophan metabolism in pregnant rats by a new tracer experimental method using a stable isotope

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L-Tryptophan (L-Trp) is one of the essential amino acids, and is a precursor for the production of several physiologically important compounds such as nicotinamide adenine dinucleotide (NAD), serotonin (5-HT), and melatonin. Recently, we developed a new method for the simultaneous detection of 15N-labelled and unlabelled L-Trp, L-kynurenine (L-Kyn), serotonin (5-HT), and quinolinic acid (QA) by gas chromatography/negative ion chemical ionization mass spectrometry (GC/NICIMS). Labelled and unlabelled versions of these four products were analysed as their acyl substituted derivatives using pentafluoropropionic anhydride and 2,2,3,3-pentafluoro-1-propanol. Products were then separated by GC and analysed by selected ion monitoring (SIM) using NICI mass spectrometry. L-[13C11, 15N2]-Trp, methyl-serotonin and 3,5-pyridinedicarboxylic acid were used as internal standards for this method. The coefficients of variation for inter-assay repeatability were found to be approximately 5.2% for L-Trp and 15N2-Trp, 17.1% for L-Kyn, 16.9% for 5-HT, and 5.8% for QA (n=2).

This method was used to determine isotope enrichments in plasma L-Trp over the course of a continuous, intravenous infusion of L-[15N2] Trp in fasting pregnant rats. Plasma 15N2-Trp enrichment reached a plateau at 120 min, and the appearance rate of free Trp (Ra) into plasma was 49.5±3.35 μmol/kg/h.

The GC/MS method was applied to determine the enrichment of 15N2-labelled L-Trp, L-Kyn, 5-HT and QA concurrently with the concentration of non-labelled L-Trp, L-Kyn, 5-HT and QA in plasma. This new method may help improve our understanding of L-Trp metabolism in vivo in pregnant animals and humans, and potentially reveal the relative contributions of these four pathways to L-Trp metabolism.

III-45 The small placenta: Neonatal and placental morphometry, hematocrit and NRBC as indicators for fetal hypoxia

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Lifelong cardiovascular and metabolic diseases may arise from adaptations to variable placental nutrient and oxygen supply relative to fetal need. The small placenta is not well-studied. In a cohort of 157 cases with placental weight (PW) < 400g sub-grouped as PW < or> the 10th centile(%), we have shown maintenance of fetal fat accretion (comparable ponderal indices) and fetoplacental weight ratio(FPR) significantly increased in PW < 10th%. We questioned whether hematocrit and/or total nRBC counts (TnRBC), each representing fetal responses to perceived hypoxia, might distinguish these groups. Our cohort of nonanomalous term singleton livebirths with PW < 400g at New York Methodist Hospital were grouped as PW< or>10th% (N=87 and N=70, respectively). Records reviewed for placental dimensions (chorionic plate surface area (CPA), disk thickness) and first CBC. Hematocrit differed between the two groups (55.6+9.7 v. 51.4+7.2, p=0.03) but total nRBC (TnRBC) did not. In PW>10th% (lower hematocrits), CPA and hematocrit were negatively correlated (r=-0.45, p=0.01). However, in PW< 10th% (higher hematocrits), only TnRBC were negatively correlated (r=-0.45, p=0.003). Higher hematocrit indicates fetal hypoxic compensation and elevated TnRBC suggesting fetal hematologic decompensation. FPR was highest in the smallest placentas (PW< 10th%) and FPR correlated with fatter newborns. Increased fetal nutrient and oxygen demand per gram PW

implied by higher FPR maintained fetal fat accretion, but only at the expense of fetal hypoxia. The correlations of hematocrit and TnRBC with CPA suggest progressive fetal hypoxia is directly proportional to CPA, a proxy for maternal uterine arterial number available for fetoplacental supply.

III-46 Plasma apelin variations during pregnancy in obese mice

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Objective: To study the plasma apelin modulations during pregnancy in obese mice.

Materials and methods: Twenty female C57Bl/6J mice were divided in two groups: 10 mice fed with show diet (C group) and 10 mice fed with high fat diet (HF group, 45% fat and 35% carbohydrate). After 3 months, we conducted an oral glucose tolerance test (OGTT) and mice were mated with male during one night. After pregnancy confirmation, blood samples were taken at E6.5, E12.5 and E18.5 after 6 hours of fasting.

Results: HF mice had an increased body weight after 40 days of exposition to high fat diet and had glucose intolerance after 3 months. There was no significant difference between fasting plasma apelin concentration between the 2 groups out of gestation. During gestation, there was an increased plasma apelin concentration at E12.5 in both groups, more pronounced in the HF group ($P< 0.001$). In obese mice, there was also an increase of insulin resistance in late pregnancy.

Discussion and conclusion: HF mice had high plasma glucose and insulin concentrations, they were glucose intolerant, but they had no plasma apelin concentrations differences between C and HF. During pregnancy, there was in our two experimental groups a rise in plasma apelin concentration at E12.5, before a return to initial levels in the HF group at E18.5. This increase coincided with the apparition of insulin resistance. Therefore, apelinergic system is modulated during gestation in obese mice, and it might be related to the change of their insulin sensitivity.

III-47 Study protocol: Metabolic programming in infancy - The role of weight velocity and body composition

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Objectives: The early weight velocity and the body composition in infancy, together with other perinatal parameters are assumed to program the metabolic system. The aim of this study is to further explore the processes behind the metabolic programming under detailed consideration of infant's nutrition, weight velocity and body composition.

Methods: The study cohort is examined twice during pregnancy (24-26 & 32-34 weeks gestation) and twice during infancy (6-8 & 14-16 weeks p.p.) and a follow up survey will be conducted at the age of one year.

During the appointments a medical, social, nutritional & obstetric history is taken and clinical examination data (e.g. weight, body composition) as well as blood, stool and breastmilk samples are obtained. The data will be examined with descriptive analysis methods.

Study design & Population: The participants eligible, for the longitudinal Pilotstudy, are healthy mothers without gestational or preexisting diabetes, who are non-smokers and have singleton pregnancies and their healthy babies are born at term (n= 100).

Study period: 01/ 2014 - 01/2016

Ethic & Funding: Ethic commission approval obtained

Funding comes from the FFG [The Austrian Research Promotion Agency]

Expected outcomes: The results will help to enhance the existing knowledge on weight velocity and metabolic programming in infancy. The special focus in this study will be on a very clear and detailed assessment of the infant's nutrition and will also add the innovative perspective of the infant's body composition.

III-48 Assessment of endothelial dysfunction in patients with metabolic syndrome

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The objective of this study is to explore changes in vascular tone regulation during a contralateral cold pressor test by performing a wavelet analysis of skin temperature fluctuations and to compare the results obtained for healthy subjects and patients with metabolic syndrome (MS).

Subjects: The control group consisted of 12 practically healthy men and women aged 39-60 years. The MS group included 10 patients aged 47-53 years (IDF).

Methods: During the cold test, the left hand was immersed in a pan with an ice-water mixture for 3 minutes. Skin temperature measurements were carried out continuously during the test on the right hand. A frequency-temporal analysis of temperature fluctuations was made using wavelet analysis. The proprietary algorithms of wavelet transform were used for filtration temperature oscillations in the myogenic (0.05-0.14 Hz), neurogenic (0.02-0.05 Hz) and endothelial (0.0095-0.02 Hz) frequency ranges.

Results: For healthy subjects exposure to cold leads to a reduction of skin temperature fluctuations in all frequency ranges, which afterwards return to their initial values. For MS patients the amplitudes of the temperature fluctuations in the endothelial frequency ranges did not recover after testing, that can be considered as impairment of vasodilatation and a symptom of endothelial dysfunction.

Conclusion: The impaired response to the cold pressor test in the endothelial frequency range for MS patients is an evidence of progressive endothelial dysfunction and can be used as the earliest predictor of vascular disorders. The created method is easy-to-use, non-invasive and appropriate for any age groups.

III-49 Impacts of prenatal FGF21 on the thermogenic gene expression in adipose tissues at neonate and adult stages

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Fibroblast growth factor 21 (FGF21) is mainly produced by the liver and its expression is transcriptionally regulated by PPAR-α. FGF21 is postulated to be a thermogenic hormone, since it has been demonstrated to be involved in the browning of white adipose tissue (WAT) and to activate thermogenic gene expression, with PGC-1α, in WAT and brown adipose tissue (BAT). The aim of this study is to investigate whether the intrauterine exposure to high levels of FGF21, by giving clofibrate (a PPAR-α agonist) to pregnant mothers, influences the thermogenic gene expression in BAT and WAT of offspring at neonate and adult stages. Pregnant C57BL/6J mice were divided into two groups to receive a control or a CF diet (0.5% clofibrate) for the whole gestational period. After delivery, all pups will be lactated by control dams, weaned on chow diet, and exposed to a high fat diet at 8-12 wk of age. The high fat diet is used to stimulate the browning of WAT. Some pregnant mothers will be killed at pregnant d18 to check the FGF21 levels in plasma and tissues. Offspring will be killed at embryonic d18, postnatal d7, 14, and 21, and at 12 wk of age to check the FGF21 levels in liver and plasma, and thermogenic gene (including Fgf21, Ucp-1, Pgc-1α, Prdm-16, Tmem26, Tbx1) expression in WAT and BAT. This study is helpful in finding a strategy to reduce obesity by increasing thermogenesis.

III-51 Potential role of ghrelin, leptin and insulin in childhood obesity programming.

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Introduction: Understanding mechanisms and factors related to early growth may give an answer for causes of obesity later in life. Ghrelin, leptin and insulin are involved in the regulation of energy balance, especially satiety level determination. This study aimed to investigate the correlation of appetite regulating hormones in cord blood with infants' anthropometric parameters in the first months of life.
Material and methods: The study covered 52 samples of cord blood. Active ghrelin and acyl ghrelin concentrations were measured by radioimmunoassay, leptin and insulin – by immunoenzymatic test ELISA. Anthropometric measurements (circumferences of head, chest, stomach, arm and thigh) were collected in 6., 8. and 9. month after birth.
Results: Total ghrelin correlated positively (p=0,026) and leptin negatively (p=0,047) with head circumference and active ghrelin positively (p=0,034) with chest circumference (increment 6. - 9. month). Total ghrelin correlated negatively with head circumference (6. (p=0,008), 8. (p=0,026) and 9. month (p=0,017)). Active ghrelin negatively correlated (p=0,027) with stomach circumference (9. month). Leptin negatively correlated (8. month) with head (p=0,018) and stomach (p=0,030), arm (p=0,019), head(p=0,026) circumference (9. month). Insulin correlated negatively with head circumference (p=0,023) in 8. month.
Conclusions: Positive correlation of ghrelin with chest circumference increment suggests the possible role of this hormone in early appetite programming. Negative correlation of cord leptin with stomach circumference may be the indicator of low body gain. Anthropometric parameters changes are dynamic in the first months of life, thus more studies seeking for a potential determinants of early childhood programming mechanisms for obesity are needed.

IV - Economics and Public Health Impact Studies/ Consumer Attitudes and Recommendations

IV-1 Alterations in androgen-regulated reproductive development in rats exposed to Ricinus communis oil during different gestation period

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Generational reproductive effects of maternal exposure to Ricinuscommunis oil (RCO) was investigated in rats. Twenty-five pregnant rats randomly assigned to 5 equal groups were treated with distilled water (control, group 1), RCO (950mg/kg p.o) during gestation days (GD) 1-7, 7-14, 14-21 and 1-21 respectively. Birth-weight, morphometric data, anogenital distance (AGD), pubertal age, sperm parameters, hormonal profile, organ-weight and histopathology were determined in first (F1) and second (F2) filial generations. Results showed a significant decrease ($p< 0.05$) in birth-weight/morphometric data in male pups from GD1-7 and 7-14. AGD decreased significantly in RCO treated F1 male. At postnatal day 90, F1 males from RCO treated rats showed significant decrease in testis, body-weight, sperm count, motility and normal morphology. Testosterone levels were significantly decreased in RCO treated F1 males which also showed testicular interstitial oedema and epididymalhypospermia. Mating, gestation, life birth, and day survival indices for control and GD 14-21 was 100% and 0% for others. Pairing F1 males from RCO treated groups and untreated females yielded 100% for all indices. Only pubertal indices were altered in F2 rats. Maternal exposure to RCO at early gestation periods impaired androgen-mediated reproductive endpoints in first generation. Ricinuscommunis oil exhibits endocrine disrupting capabilities.

IV-2 Testicular and epididymal histomorphometric assessment in F1 male Wistar rats maternally exposed to Ricinus communis oil at various stages of gestation

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Fetal programming hypothesis presupposes that stimulus or insult acting during critical periods of uterine growth and development may permanently alter tissue structure and function. Ricinuscommunis oil (RCO) has been shown to possess laxative, labour inducing and estrogenic properties. Therapeutic dose of Ricinuscommunis oil (RCO) 950mg/kg BW was administered to pregnant Wistar rats at gestation days GD 1-7, 7-14, 14-21 and 1-21 respectively. Epididymis in treated compared to the control male offspring showed no visible lesions except for sparse epididymal luminal content in male offspring from GD1-7, GD 7-14 and GD1-21. Moderate interstitial oedema was present in male offspring from GD1-7 and GD1-21. Seminiferous tubular diameter (STD) significantly ($p< 0.001$) increased in F1 males from GD1-7, 7-14, 14-21 relative to control group. Seminiferous tubular epithelial height (SEH) significantly ($p< 0.001$) decreased in F1 males from GD1-7,7-14 and 1-21. Seminiferous luminal diameter (SLD) increased significantly ($p< 0.001$) in F1males from GD1-7, 7-14, 14-21 and 1-21. Epididymal tubular diameter (ETD) significantly ($p< 0.01$) increased in F1 males from GD1-7, 7-14, 14-21. Epididymal tubular epithelial height (EEH) significantly ($p< 0.001$) increased in F1 males from GD1-7 and GD7-14. The epididymal luminal diameter (ELD) however increased significantly ($p< 0.001$) only in F1 males from GD1-7. Maternal RCO exposure at different gestation periods impaired negatively histomorphometry of the testis and epididymis in male offspring.

IV-3 Morphometric variables of offspring of quassia amara treated albino male rats

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Quassia amara is a medicinal plant with various pharmacological properties. The bioactive compound quassin is used as flavoring in food and beverages. Reproductive toxicological action of Q. amara is well documented but no information exists on its effect on prenatal programming.

Adult male rats (180-200g, n=5) were administered single daily oral dosage of Q. amara extract (100mg/kg) for 6 weeks. A control group received distilled water. After 5 weeks of treatment, female rats were cohabited with the male for 7 days, at the ratio of 2:1. Mating was confirmed by presence of spermatozoa in all vaginal smear. Morphometric indices of all offspring were recorded on postnatal day one. They were also examined for any sign of abnormality or physical defect.

Fertility was zero in four out of the five treated rats. The females that cohabited with the fertile treated male gave birth to pups of varying sizes (6 and 9). However, fertility was four out of the five control male rats and the pregnant females had 9 pups each. No visible physical defect was observed on all offspring. Anogenital distance of the male offspring of the treated rats was significantly shorter than male offspring of the control, while anogenital distance of female offspring showed no statistical difference. Head diameter and body length was also significantly lower in offspring of the treated rats. However, weight, abdominal diameter and male: female ratio of offspring were not statistically different. The results indicate that Q. amara may alter the developmental programming of sperm cell.

IV-4 Customer preferences regarding purchase of foods and associations with socio-demographic characteristics

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Food behaviours play an important role in development of disease. Thus it is essential to follow proper food behaviours to lead a healthy life.

The general objective of this study was to determine the customer preferences regarding purchase of foods in an urban population.

A descriptive cross-sectional study was carried out among 384 consumers, who visited selected public markets at Kirulapone and Manning Place, Wellawatte, Colombo. An interviewer administered questionnaire was used and data were analyzed using SPSS(15.0 version). The majority of the population was females (65.1%) in the age group of 20-35 years (54.2%) and 54.4% were Tamils in this population. It was observed that the most important five factors which influence the customer preferences; were distributed as follows, nutrition (36.2%) was ranked the highest followed by taste (24.2%), cost (17.7%), brand name (12.2%) and convenience (8.6%). A statistically significant ($P< 0.05$) difference on food preferences were observed with ethnicity and age groups, whereas gender ($P>0.05$) had no significant difference with food preferences. Approximately 65 % of the population considered only expiry dates of the food labels before purchasing food products. Reference of food labels too had significant ($P< 0.05$) differences with ethnicity and gender, whereas age groups ($P>0.05$) showed no significant association regarding same.

Nutritional content of food, taste, cost, brand name and convenience were identified as the most important factors when purchasing food by the present study population. Expiry date was the major factor which was considered from the food label before selecting a food item.

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Coffee Breaks / Lunch
Coffee breaks and a light lunch will be available during the official coffee / lunch break times (please see "Snack Bar" and "Lunch Area" on the floor plan) for registered participants wearing their badge. A seating area is located on the 2nd floor

Conference Language
All lectures and discussions will be held in English. There will be no simultaneous translation.

Conference Venue
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Conference Hours

Thursday, 13 March 2014	10.00 - 17.50
Friday, 14 March 2014	08.20 - 18.05
Saturday, 15 March 2014	09.00 - 14.00

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Registration is possible at the registration desk located on the first floor of the auditorium section. On-site registrations are subject to availability.

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The media check is located in lecture hall I on the 1st floor.

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Important Information

- Oral presentations must be held by the first author of the submitted abstract.
- Presentations should be created in PowerPoint 2010, Format: 4:3 (1024 x 768).
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- No personal laptops may be used as it may not be compatible with the equipment onsite.
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New Investigators' Award
The New Investigators' travel grants will be awarded to the best submitted abstracts by New Investigators. The New Investigators' awards will be presented during the Farewell Note at the end of the conference on Saturday, 15 March. The winners have been informed separately.

Poster Exhibition
The poster areas are located on the 1st and on the 2nd floor of the auditorium section (please see floor plan on page 18):

I Prevention and Intervention
II Epidemiology
III Mechanisms
IV Economics and Public Health Impact Studies / Consumer Attitudes and Recommendations

Posters must be mounted on Thursday, 13 March by 13.15. Presentation of the poster is requested during the whole conference as the poster viewing is scheduled accompanying the entire programme. Posters of distinction will be introduced by the main authors within the Guided Poster Session on Friday, 14 March from 13.25 – 14.25. Posters must be removed on Saturday, 15 March by 15.00 at the latest. Posters which have not been removed by this deadline will be subject to disposal. Neither the Scientific Committee nor the venue is responsible for removing and returning 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, March 13 from 8.30 – 12.30.

Guided Poster Session
The posters of distinction will be introduced by the first authors during the Guided Poster Session on Friday, 14 March from 13.25 to 14.25. After a short introduction by the Chair each poster will be presented in a 5 minute talk. The authors are requested to be in the poster area at least 15 minutes before the guided tour starts.

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Please take the subway line U1 (direction Innsbrucker Ring) or U2 (direction Neuperlach Süd) to Sendlinger Tor (one stop from the Hauptbahnhof/central station) and change to the subway line U6, terminus *Klinikum Grosshadern*.
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All session halls are located on the 1st floor.

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The wardrobe can be found next to the main entrance of the auditorium section. 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

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

Location:	Alter Rathaussaal Marienplatz 15, 80333 München Entrance on the footpath between Marienplatz and Tal (all fast trains, subway and fast train station „Marienplatz", subway line U3 or U6)
Date/Time:	Thursday, 13 March 2014 at 19.00
Price per person:	included in the registration fee separate registration necessary (subject to availability)
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On Friday night we will celebrate a Bavarian Evening with traditional food and entertainment in a relaxed atmosphere.

Location:	Hofbräukeller Innere Wiener Straße 19, 81667 München (fast train / S-Bahn station „Rosenheimer Platz", tram 16 „Wiener Platz", subway station „Max Weber Platz, U4/U5)
Date/Time:	Friday, 14 March 2014 at 19.30
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References:

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