N&G 2023 - Invited Speakers Abstracts

IS001 / #4

OPENING CEREMONY & KEYNOTE LECTURE
03-30-2023 12:30 - 13:15

HOW SHOULD WE ANALYSE LONGITUDINAL GROWTH?

Tim J Cole
UCL Great Ormond Street Institute of Child Health, Population, Policy And Practice Programme, London, United Kingdom

During infancy and puberty, longitudinal growth in height or weight is complicated to model because the growth curves representing individual growth patterns vary considerably in shape. A popular way to analyse such data is to convert the measurements to z-scores—it removes the age trend and linearises the curves. However it also discards useful information about the shape of the growth curve and complicates the analysis of growth during puberty. This talk focuses instead on the measurement scale, and describes a relatively novel growth model called SITAR (Cole et al, 2010).

Two general features of the growth pattern are useful to summarise: a) the shape of the mean growth curve, and b) the nature and extent to which individuals deviate from the mean curve. But this poses a problem—how can one average curves that differ in shape? The trick is to assume that the curves all have the same underlying shape, and that they differ from each other only in simple ways.

SITAR achieves this by estimating a mean growth curve from which individual growth curves differ in just three respects: size (i.e. the extent to which the individual is consistently taller/shorter or heavier/lighter than average); timing (by how much their age at peak growth velocity is earlier or later than average), and intensity (by how much their average growth velocity is higher or lower than average). So individual growth patterns are summarised on three scales: size = small/big, timing = early/late and intensity = slow/fast. Geometrically, size and timing correspond to shifting the curve down/up and left/right, while intensity rotates the curve. SITAR (SuperImposition by Translation and Rotation) is a nonlinear mixed effects model that estimates size, timing and intensity as random effects, while the mean growth curve is a natural cubic spline. It differs from growth models like Jenss-Bayley, Preece-Baines or Karlberg's ICP which use parametric forms of curve—the advantage of a cubic spline curve is that its shape is defined purely by the data, and hence can be relatively complex, unconstrained by a prespecified mathematical form.

Applied to studies of height in puberty, SITAR fits the data extremely well. The residual standard deviation is typically less than one tenth of the population standard deviation, so the model explains over 99% of the variance. It estimates mean curves for distance and velocity, from which mean final height and mean ages and values of height velocity at take-off and peak can be extracted. It also compares growth summary statistics across two or more groups. Published examples of SITAR include randomised clinical trials testing the effect on attained height of oxandrolone in girls with Turner syndrome, and of calcium supplementation in boys and girls from The Gambia subsisting on a low calcium diet.

Separately SITAR addresses questions concerning the life course, where individual growth patterns in childhood—as summarised by size, timing and intensity—are viewed as exposures relating to later life adverse outcomes. An example here links the age at peak height velocity to bone health in later life, showing that an early puberty is associated with stronger bones at age 60.

SITAR is very effective at summarising the complexity of growth. This may be because it mimics the biology of growth as championed by J M Tanner, focussing on the growth spurt in terms of peak velocity and age at peak velocity.

IS002 / #14

PLENARY SESSION 01: NEW TREATMENTS FOR OBESITY
03-30-2023 13:15 - 14:45

PHARMACOTHERAPY IN CHILDHOOD OBESITY- DOES GLP-1 RECEPTOR AGONIST IS A "GAME CHANGER"

Shlomit Shalitin
The national institute of endocrinology and diabetes, Schneider children's Medical Center of Israel, Petavh Tikva, Israel

The increasing number of young patients with obesity worldwide is a major challenge for health care systems in many countries.

The gold standard for the treatment of obesity remains a multimodal conservative treatment regime to improve physical activity & reduce caloric intake.

Unfortunately, with this conservative treatment regime, the impact on body weight is overall modest and the majority of patients regain weight. This is the reason why there is an urgent need to establish new treatment strategies for children and adolescents with obesity in order to reduce the risk for the development of comorbidities, and increased mortality later in life.

The leptin-melanocortin pathway and the incretin system are deeply involved in a complex regulation of food intake. One of the incretins is the glucagon like peptide-1 (GLP-1). Like human GLP-1, liraglutide (Saxenda®) is a glucagon- like peptide 1 receptor (GLP-1R) agonist that works on glucose metabolism and body weight due to various mechanisms: promoting insulin secretion from pancreatic β-cells; reducing glucagon secretion from pancreatic α-cells; improving insulin sensitivity; reducing gastric emptying; and improving central appetite regulation.

A large randomized, double-blind placebo- controlled trial, published by Kelly et al., which consisted of a 56-week treatment period and a 26-week follow-up period evaluated the efficacy and safety of liraglutide (3.0 mg) or placebo subcutaneously once daily, in addition to lifestyle therapy among adolescents 12-18 years of age with obesity and a poor response to lifestyle therapy. The results of the study showed that liraglutide was superior to placebo with regard to the change from baseline in the BMI standard-deviation score at week 56, with a significant higher percentage of patients that achieved a reduction of at least 5% in the BMI in the liraglutide group compared with the placebo group. Major side effects included gastrointestinal symptoms.

After this publication, the Saxenda® has been approved by the FDA in 2021 as an anti-obesity drug in addition to lifestyle therapy in adolescents. Further data from real- life setting are needed to assess the use of the medication in larger number of pediatric patients with obesity, in order to evaluate its efficacy and safety in the long-term and the possibility of prevention of obesity related comorbidities.

IS003 / #16

PLENARY SESSION 01: NEW TREATMENTS FOR OBESITY
03-30-2023 13:15 - 14:45

NEW TREATMENT FOR RARE GENETIC OBESITY DISORDERS

Erica Van Den Akker
Erasmus MC Sophia Children's Hospital, Pediatrics, Div Pediatric Endocrinology And Obesity Center Cgg, rotterdam, Netherlands

Abstract Body: Genetic obesity disorders are severe and disabling disorders with a variety of accompanying symptoms or features. These disorders are rare to extremely rare and can be difficult to diagnose. Genetic obesity disorders are more often diagnosed in children than in adult patient groups. Genetic obesity reflects a heterogeneous group of conditions. They are classically divided into non-syndromic and syndromic obesity. Non-syndromic genetic obesity disorders are often caused by a single gene defect leading to defective leptin-melanocortin pathway. Severe obesity classically presents in the first years of life. Syndromic genetic obesity differs from non-syndromic, as they have additional symptoms, apart from obesity, like neurodevelopmental disorders and/or polymalformative syndrome. Children with rare genetic obesity disorders present with insatiable behavior (hyperphagia) and early-onset obesity. The cause is a genetic defect disrupting the signaling through the melanocortin-4 receptor (MC4R) pathway, in the hypothalamus. Traditional lifestyle interventions are an important basis of treatment but patients are often treatment resistant. In addition to supportive lifestyle interventions, novel pharmacotherapeutic treatment options have become available. Case series have been described using dextroamphetamine or GLP1 agonist. After EMA approval based on clinical trials, patients with specific genetic obesity disorder can now be treated with the MC4R agonist from the age of 6. In conclusion drugs targeting central brain pathways of weight regulation and energy expenditure provide new and promising treatment options for patients with genetic obesity disorders. References: Hampi S., Hassink S. et al. Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity. Pediatrics(2023),151,https://doi.org/10.1542/peds.2022-060640 2020 Webinar Rare EndoERN MTG growth and obesity. Disorders in the leptin-melanocortin pathway. 7juli2020: https://www.youtube.com/watch?v=isFixGGQjS8 Lotte Kleinendorst*, Ozair Abawi, * Bibian van der Voorn, Mieke H.T.M. Jongejan, Annelies E. Brandsma, Jenny A. Visser, Elisabeth F. C. van Rossum, Bert van der Zwaag, Marielle Alders, Elles M. J. Boon, Mieke M. van Haelst, Erica L.T. van den Akker. Identifying underlying medical causes of pediatric obesity: Results of a systematic diagnostic approach in a pediatric obesity center. https://doi.org/10.1371/journal.pone.0232990. Martin Wabitsch, Sadaf Farooqi, Christa E Flück, Natasa Bratina, Usha G Mallya, Murray Stewart, Jill Garrison, Erica van den Akker, Peter Kühnen. Natural History of Obesity Due to POMC, PCSK1, and LEPR Deficiency and the Impact of Setmelanotide. April 2022Journal of the Endocrine Society. DOI: 10.1210/jendso/bvac057 Van Schaik J, Schouten-van Meeteren AYN, van der Akker ELT, van Santen HM. Dextroamphetamine treatment in children with hypothalamic Obesity. Front Endocrinol (Lausanne). 2022 Mar 9;13:845937. Doi: 10.3398/fendo.2022.845937 Welling M, de Groot, Kleinendorst, van der Voorn, Burgerhart, van der Valk, van Haelst, van den Akker ELT,

van Rossum. Effects of glucagon-like peptide-1 analogue treatment in genetic obesity: A case series. Clin Obes. 2021 Dec;11(6):e12481. https://doi.org/10.1111/cob.12481 Clément K*, van den Akker E* , Argente J, Bahm A, Chung WK, Connors H, De Waele K, Farooqi IS, Gonneau-Lejeune J, Gordon G, Kohlsdorf K, Poitou C, Puder L, Swain J, Stewart M, Yuan G, Wabitsch M*, Kühnen P*. Efficacy and safety of setmelanotide, an MC4R agonist, in individuals with severe obesity due to LEPR or POMC deficiency: single-arm, open-label, multicentre, phase 3 trials. Setmelanotide POMC and LEPR Phase 3 Trial Investigators. Lancet Diabetes Endocrinol. 2020 Dec;8(12):960-970. doi: 10.1016/S2213-8587(20)30364-8. Epub 2020 Oct 30. PMID: 33137293.

IS004 / #11

PARALLEL SESSION 01: THE KEY ROLE OF NUTRITION IN SHORT BOWEL SYNDROME
03-30-2023 15:00 - 16:00

GROWTH IN SHORT BOWEL SYNDROME (SBS)

Olivier Goulet
Paris-Cité University, Necker Hospital, Paris, France

Abstract Body: Although the care of children with SBS-IF has improved significantly in recent years, their nutritional status is frequently affected by the limited absorption of nutrients. About 50% of the children may have short stature for age, and one-third of them may have low bone mineral density. Children with inflammatory conditions might be at greatest risk of growth failure and inflammation might be a predictor of short stature in the long term. Optimal growth in SBS children needs to cover energy requirements including energy for basal metabolic rate or resting energy expenditure (REE), physical activity, growth and the metabolic response to feeding. In children with SBS-IF faecal energy losses are greater compared to healthy children. Furthermore, energy losses vary between patients according to the anatomy while having a remnant colon represents a potential for energy salvage. REE may be measured by indirect calorimetry or by using predictive equation such as Schofield formula. The PN dependency index (PNDI) is the ratio between non-protein-energy intake (NPEI), provided by PN for achieving normal or catch-up body weight gain, and REE) (PNDI = NPEI/REE). Protein (nitrogen) intake is established according to recommendations and adapted to the Nitrogen/Energy ratio (1gr Nitrogen for 200-250kcal). Given the intestinal malabsorption that characterizes the SBS, it is inappropriate to consider that the sum of enteral and parenteral nutritional intakes corresponding to RDAs can be optimal. We have observed in weaned off PN SBS pediatric patients, a syndrome we call the “overloaded gut syndrome” (abdominal distension, digestive dyscomfort and failure to thrive) resulting from forced tube feeding in insufficiently adapted remaining intestine. This requires to resume PN for a while and discuss non-transplant surgery and/or GLP-2 analog treatment. Serum citrulline is though as a helpful marker of intestinal absorption, however effective cut off levels cannot be extrapolated. Changes in serum citrulline levels along the process of adaptation is correlated with the PNDI reflecting the changes in intestinal mucosa growth and may be used as a reliable predictive factor of PN weaning. Beside inappropriate protein-energy intake, other factors may cause failure to thrive such as sodium deficiency from high stool output, small intestinal bacterial overgrowth, chronic metabolic acidosis (e.g. D-Lactic), IFALD, and repeated catheter related blood-stream infections. Nutritional status should be monitored to adapt the nutritional support. It includes body weight and length gain velocity as well as BMI. Height curves should always be weighted upon genetic target size. Body composition is helpful and may be easily assessed by using dual X-Ray Absorptiometry (DXA) that measures also bone mineral density. Data on final adult height are scarce while it is greatly influenced by the long term management and follow up of SBS pediatric patients. One of the objectives of an optimal management is to reach or even exceed the genetic target size.

IS005 / #13

PARALLEL SESSION 01: THE KEY ROLE OF NUTRITION IN SHORT BOWEL SYNDROME
03-30-2023 15:00 - 16:00

NEW FRONTIERS TO IMPROVE ABSORPTION AND PREVENT COMPLICATIONS

Lorenzo Norsa
ASST Papa Giovanni XXIII, Pediatric Hepatology, Gastroenterology And Transplantation, Bergamo, Italy

Short bowel syndrome (SBS) is the leading cause of intestinal failure (IF) in children. The mainstay of treatment for IF is parenteral nutrition (PN).

SBS-IF may be reversible or irreversible, depending on several factors such as the underlying cause of SBS, the length of the remaining intestine and treatment used to develop or restore intestinal autonomy.

Numerous factors determine SBS prognosis and duration of PN dependency: the underlying diagnosis, the type and condition of intestinal segments preserved, the presence/absence of the ileo-cecal valve (ICV) and/or colon, a long-term enterostomy versus a primary anastomosis, any associated motility disorders, especially in intestinal atresia and gastroschisis, the number of surgical procedures, as well as the age of the patient at the time of surgery.

Long term follow of SBS-IF may be affected by multiple complication which are linked or not to long term home-PN. Even if impressive progress has been made in the latest decade in dealing with home-PN, some of those complication may be evolutive and irreversible and expose to risk of nutritional failure which may require intestinal transplantation.

The aim of the long-term treatment of SBS-IF should, thus, be multiple: on one hand, aiming to improve intestinal absorption to facilitate PN weaning; on the other hand, aiming to prevent from the very beginning the onset of complications which would highly impact on SBS-IF prognosis.

The aim of the current lecture will be to analyze all recent advancement in medical care which allowed to improve intestinal absorption rate and to avoid as much as possible complications in children with SBS-IF.

IS006 / #17

PLENARY SESSION 02: FOOD ALLERGY MANAGEMENT AND PREVENTION
03-30-2023 18:15 - 19:15

WHAT IS NEW IN THE 2022 FOOD ALLERGY MANAGEMENT GUIDELINES

Hania Szajewska
The Medical University of Warsaw, Department Of Paediatrics, Warsaw, Poland

Food allergy remains common in children. However, the diagnosis and management of food allergy can vary between clinical practice settings. To promote the best clinical practices, worldwide, scientific organizations or groups of experts provide guidelines. Even if such documents are typically based on systematic reviews, the guidelines often differ. This presentation will discuss the most recent documents, including: 1) the 2021 guideline from the Global Allergy and Asthma European Network (GA^2LEN), focusing on food allergy in general, and 2) two 2022/2023 documents focusing on cow's milk allergy (CMA), which remains the most common food allergy in infants and young children, i.e., the World Allergy Organization DRACMA (Diagnosis and Rationale for Action against Cow's Milk Allergy) guidelines and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guidelines. Key similarities and differences will be discussed.

Dietary management of CMA requires choosing the best suitable cow's milk substitute for use in infancy and beyond. This presentation will discuss how and when to choose a suitable substitute, which is dependent on many factors. These factors include the infant's symptomatic presentation, age, and nutritional needs, the latter which may include a hypoallergenic formula, maternal elimination diet if the infant is symptomatic during exclusive breastfeeding, or plant-based formulas. The question as to what to do when recommendations from medical societies are not in agreement will be addressed. The gaps in the current evidence will be presented and discussed with recommendations for future research and/or clinical trials to address these gaps.

IS007 / #19

PLENARY SESSION 02: FOOD ALLERGY MANAGEMENT AND PREVENTION
03-30-2023 18:15 - 19:15

UPDATE IN FOOD ALLERGY PREVENTION THROUGH NUTRITION

Yvan Vandenplas
Vrije Universiteit Brussel (VUB), Uz Brussel, Kidz Health Castle, Brussels, Belgium

Abstract Body: The many confounding variables in the pathogenesis of allergy may contribute to the differences between animal studies, where all variables are controlled, and trials in infants. The mode of delivery, perinatal administration of antibiotics to the mother or infant and feeding all influence the GI microbiota and the risk of developing allergy. An important feature characterizing epigenetically-mediated processes is the existence of a time frame where the induced effects are the strongest and, therefore, most crucial. Breastfeeding should be promoted for its multiple benefits, although its preventive effect on allergy has not been consistently documented There is no convincing scientific evidence that the avoidance or delayed introduction of CM-based formula reduces or increases the risk of CMA in infants considered at high risk of allergic diseases. Complementary bottles given at maternity hospitals to newborns who will later be exclusively breastfed increases the risk of developing CMA. For infants with a documented family history of allergic disease who cannot be exclusively breastfed, there is insufficient evidence to recommend the routine use of pHF, eHF-Whey, eHF-Casein for preventing CMA.In some prevention trials randomisation was allowed up to the age of 1 month, meaning that a number of infants were fed intact CMP before inclusion in the trial. Sensitisation to CMP may also develop through skin contact. It should be considered whether a pHF-W with effectiveness in the reduction of the risk of allergic manifestations such as atopic eczema demonstrated in allergy prevention studies, is chosen until complementary food is introduced. A reduced cumulative incidence of atopic dermatitis was found among infants who received a pHF-W or eHF-C versus CM formula during a 20-year follow up. In addition, after 16 to 20 years of follow-up, the prevalence of asthma after puberty in a high-risk population was lower in both the eHF-C and pHF-W groups. There is insufficient evidence to recommend the use of probiotics, prebiotics or synbiotics studied so far for CMA prevention. There is insufficient evidence to recommend the use of long chain poly-unsaturated fatty acids (LCPUFAs) for CMA prevention.Vitamin D supplementation during pregnancy, during lactation or infancy had little to no effect on food allergy in early childhood.

IS008 / #54

NEW INSIGHTS INTO BIOLOGY OF HUMAN MILK
03-31-2023 8:00 - 8:25

NOVEL INSIGHTS ON THE IMPORTANCE OF COLOSTRUM FOR HEALTHY DEVELOPMENT

Valerie Verhasselt
The University of Western Australia, Lrf Centre Of Research For Immunology And Breastfeeding (cibf), Perth, Australia

Among mothers that initiate breastfeeding, at least one in three will not optimally breastfeed during the first days. They will either initiate breastfeeding more than one hour after delivery and/ or will provide supplement feeding. Besides exposing the child to potential pathogens and /or allergens, this worldwide practice will result in colostrum withdrawal for the neonate. Colostrum, the first fluid produced by the mammary gland, is rich in protein, immune and growth factors. It also has the potential to shape the establishing gut microbiota through its abundance of oligosaccharides and antimicrobial factors. While there is evidence pointing to the importance of colostrum for the prevention of early mortality in low and middle-income countries, there is a lack of knowledge on the long-term health impacts of insufficient colostrum intake. To fill this gap, we have developed a unique pre-clinical model where we compare the development of mice breastfed physiologically to mice breastfed by a dam that differed by the time of initiation of breastfeeding.

Colostrum deprivation at birth caused significant growth failure that persisted into adulthood. Colostrum ignited the somatotropic hormone axis to ensure both weight gain and longitudinal growth. We further found that colostrum at birth was required for the postnatal expansion of Innate lymphoid type 2 cells (ILC2) by promoting their survival. Colostrum-driven ILC2 expansion was necessary for successful control of gut helminth infection in infant mice. Preliminary data in humans corroborated this finding. Given the known importance of the gut microbiota in health and disease, we evaluated the role of the microbiota in the mediation of colostrum's beneficial health effects. While the gut microbiota diversity and composition were altered in mice lacking colostrum at birth, we demonstrated in germ-free mice that the effect of colostrum deprivation was recapitulated in the absence of microbes.

In conclusion, this talk will highlight that colostrum may represent a missing link for healthy development. Our data revealed that colostrum at birth was critical for later prevention of undernutrition and helminth infection, both representing a major burden of disease in children. They also stressed that the diet in early life can profoundly affect development independently of the microbiota. This unexpected finding suggests that microbiota interventions may not necessarily represent the major focus of new strategies to foster healthy development in early life. Evidence-based promotion of colostrum feeding and the design of colostrum-inspired supplements may change the lives of many children.

IS009 / #20

PARALLEL SESSION 02: VEGAN DIETS IN INFANCY AND CHILDHOOD
03-31-2023 10:30 - 12:00

HEALTH BENEFITS AND RISKS OF VEGAN DIETS IN CHILDREN

Malgorzata Agnieszka Desmond
Great Ormond Street Institute of Child Health UCL, Population, Policy & Practice, London, United Kingdom

Plant-based diets are increasingly recommended for personal health and planetary health; however, evidence on the health and dietary intakes of children on vegetarian, and particularly on vegan diets has been limited. Vegetarians and vegans restrict intake of whole food groups. This is of particular concern in children, whose nutrient and energy needs are higher relative to body weight and whose growth might be impaired by nutrient deficiencies at sensitive periods of development. Until recently, data on the health and nutritional intake of children on meatless diets have come from studies of heterogenous design, and related predominantly to vegetarian children. Only two studies document the dietary intake of children on vegan diets and one is from the 1980ties. Until 2021 there was no data on blood biomarker status for this group. The sparsity of evidence contributes to inconsistencies between medical and nutrition organisations' statements regarding the safety of vegan diets in childhood.

The presentation will discuss the existing evidence on this topic, in particular the results of a cross-sectional study of 63 vegetarians, 52 vegans, and 72 omnivores aged 5-10 years old, conducted to quantify the differences in several health outcomes and micronutrient status between these three groups in a cohort of healthy Polish children (Desmond et al. 2021). The focus will be on the nutritional blood biomarkers of the data. Additionally, soon to be published data on the dietary intakes and the risk of inadequate nutrient intakes of the same cohort will be presented. Compared to omnivore children, vegans had increased risk of nutritional deficiencies and increased risk of inadequate nutrient intakes. The results of the vegetarian children were in the same direction, however less pronounced.

The implications of these findings will be elaborated on and the recommendations suggested on how to customize the advice to vegans compared with vegetarians so that the established benefits of these diets are maximized and the risks minimised in the paediatric population.

Desmond M.A., Sobiecki J.G., Jaworski M., Płudowski P., Antoniewicz J., Shirley M.K., Eaton S., Książyk J., Cortina-Borja M., De Stavola B., et al. Growth, Body Composition, and Cardiovascular and Nutritional Risk of 5- to 10-y-Old Children Consuming Vegetarian, Vegan, or Omnivore Diets. Am. J. Clin. Nutr. 2021;113:1565.

IS010 / #21

PARALLEL SESSION 02: VEGAN DIETS IN INFANCY AND CHILDHOOD
03-31-2023 10:30 - 12:00

CONTRIBUTION OF CHILD NUTRITION TO THE BALANCE BETWEEN PLANETARY AND HUMAN HEALTH

Luis A Moreno[1], Leandro Cacau[2]
[1]Universidad de Zaragoza, Genud Research Group, Zaragoza, Spain, [2]University of São Paulo, Department Of Nutrition, School Of Public Health, São Paulo, Brazil

Food consumption may influence environmental impact and this could start during childhood and adolescence. According to FAO/WHO (2019), Sustainable Healthy Diets are dietary patterns that promote all dimensions of individuals' health and wellbeing. Planetary boundaries provide levels of perturbation that are believed to ensure that the Earth System is kept in conditions that are favourable for humanity. Footprints are indicators of pressure of human activities on the environment; their quantification is based on life cycle thinking along the whole supply chain (from producer to consumer) and they can be quantified at any stage of the supply chain. Systems affected by food production are climate change, biodiversity loss, land system change, freshwater use and nitrogen and phosphorus flows. Food-systems-related activities, account for 20–30% of total greenhouse gas emissions (GHGEs) and 70% of freshwater use, contributing both significantly to climate change. Considering only the environmental impact, the diets without animal products appears to be the optimal diet, producing the lowest level of GHGEs; however, when considering other aspects like nutrient intake, food availability and diversity it is possible to achieve the same environmental impact consuming some meat and dairy food products. In this respect, the Mediterranean Diet is a plant-based diet, with little to moderate amounts of foods from animal sources and it is considered one of the healthiest dietary patterns. Adherence to the Mediterranean Diet was also shown to reduce GHGEs (72 %), land use (58 %), energy consumption (52 %) and water consumption (33 %). Composing healthy diets with a low environmental impact is quite complex, as every food contains a different mixture of nutrients and has different values for environmental indicators. Animal-based products make a significant contribution to the intake of essential nutrients like Fe, Se, Zn, Ca, thiamin, vitamin B12 and vitamin D. Nutritional challenges are foreseen for these micronutrients in case of limitation of meat and dairy products consumption, and this may be especially important for children because of growth requirements. The EAT-Lancet Commission released a reference sustainable diet to improve human health and respect the planetary boundaries. A healthy and sustainable diet proposed by the EAT-Lancet may play a positive role in the cardiovascular health and in some cardiometabolic risk factors, contributing to the findings regarding the benefits of the adoption of a healthy and sustainable diet. The Planetary Health Diet Index (PHDI) was developed with the purpose of evaluate the adherence to this reference diet. In European adolescents, a 10-point increment in the PHDI was associated with a lower probability of a non-ideal cardiovascular health index (OR 0.84, [95% CI: 0.75, 0.94]) among European adolescents, after adjusting for age, sex, socio-economic status and total energy intake. At individual level, a 10-point increment in the PHDI was associated with a lower probability of being a smoker (OR: 0.93 [0.87, 0.98]), lower odds of a poor physical activity level (OR: 0.87 [0.82, 0.93]), lower probability of a poor

diet (OR: 0.54 [0.35, 0.85]), lower odds of high blood pressure (OR: 0.87 [0.79, 0.96]), and a lower probability of high blood cholesterol (OR: 0.88 [0.78, 0.99]). A shift to healthier diets requires that the necessary foods be both available and affordable for low-income populations. Dietary guidelines need to be adapted to children needs and specific public health context.

IS011 / #22

PARALLEL SESSION 02: VEGAN DIETS IN INFANCY AND CHILDHOOD
03-31-2023 10:30 - 12:00

VEGETARIAN, VEGAN OR OMNIVORE DIETS. GROWTH, BODY COMPOSITION AND CARDIOVASCULAR AND NUTRITIONAL RISKS

Jonathan Wells
UCL Great Ormond Street Institute of Child Health, Institute Of Child Health, London, United Kingdom

Abstract Body: Plant-based diets are increasingly recommended and practiced globally. While promoted for planetary sustainability and animal welfare, plant-based diets may also have immediate and long-term health benefits. In adults, studies have shown that vegetarians (VG) and vegans (VN) have lower risk of cardiovascular disease compared to omnivores (OM). In turn, it is increasingly recognised that the risk of cardiovascular disease in adult life may be shaped by nutrition and growth patterns in childhood. The process of atherosclerosis commences in early life, and progresses in relation to classical cardiovascular risk factors that, along with dietary habits, tend to track into adult life. However, until recently, the associations of VN and VG diets with growth, body composition and cardiometabolic risk markers in young children received surprisingly little attention. At a conceptual level, plant-based diets might impact cardiometabolic health in children in several ways. First, any constraints on growth might undermine the development of homeostatic metabolic capacity, referring to physiological traits such as organ size, structure and function that promote long-term cardiometabolic and musculo-skeletal health. Second, unhealthy diets might impact blood biochemistry relating to glucose-insulin and lipid metabolism or markers of inflammation. Third, differences in fat deposition and distribution may impact cardiometabolic physiology. Recent studies indicate small decrements in the height of VN relative to OM children in early life, that may amplify slightly in mid-childhood. However, it is not yet clear whether VN children will stay smaller as adults, or whether they are simply reaching their adult height at a slower rate. Of potentially greater concern, both VN and VG children may accumulate lower bone mineral density, which might increase the risk of osteoporosis in old age. VN children may have lower absolute adiposity and a lower risk of overweight compared to OM children. VN children may also have a more favourable blood lipid profile, and lower inflammatory markers. However, plant-based diets are not necessarily of high quality and in one study of VG children were associated with greater cardiometabolic risk compared to OM children. Overall, research suggests that plant-based diets can potentially benefit children's cardiometabolic health, with important implications for the primordial prevention of adult cardiovascular disease. Some benefits appear greatest in VN children, particularly those relating to adiposity, however there are also potential costs in terms of long-term skeletal health. Moreover, VN and VG children need guidelines on how to eat healthfully, beyond advice on supplementation.

IS012 / #168

PLENARY SESSION 03: YEARBOOK
03-31-2023 14:00 - 15:15

MALNUTRITION AND CATCH-UP GROWTH DURING CHILDHOOD AND PUBERTY

Michal Yackobovitch - Gavan[1,2], Naama Fisch-Shvalb[1,3], Zulfiqar A Bhutta[4,5]
[1]Schneider children's medical center, Endocrinology And Diabetes, Petach Tikva, Israel, [2]Tel Aviv University, Epidemiology And Preventive Medicine, School Of Public Health, Tel Aviv, Israel, [3]Tel Aviv University, Sackler School Of Medicine, Tel Aviv, Israel, [4]The Hospital for Sick Children, Centre For Global Child Health, Toronto, Canada, [5]The Aga Khan University, Center Of Excellence In Women And Child Health, Karachi, Pakistan

In 2020, approximately 149.2 million children, or 22%, of all children under 5 years of age across the globe were estimated to be to be affected by stunting, and 45.4 million children under 5 by wasting, of whom 13.6 million were severely wasted [1]. Although the rates of both stunting and wasting have been significantly reduced over the past couple of decades, these numbers are still staggering. According to WHO, the number of people affected by hunger globally have increased by 150 million since the outbreak of COVID-19 [2]. Amidst climate changes, economic instability and growing inequalities, achieving the global targets of reducing the number of children with stunting to 104 million by 2025 and to 87 million by 2030 seems more challenging than ever.

This chapter reviews the most recent data on childhood malnutrition and catch-up growth, published between July 1, 2021 and June 30, 2022. The chapter addresses several main topics, including the etiology and mechanisms of malnutrition in children, adolescent nutrition, Interventions in childhood malnutrition and late outcomes of malnutrition.

References

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IS013 / #162

PLENARY SESSION 03: YEARBOOK
03-31-2023 14:00 - 15:15

STUNTING OF GROWTH IN DEVELOPING COUNTRIES

Joyceline Kathembe[1], Janet Tapkigen[2], Martha Mwangome[3], Andrew Prentice[4], Helen Nabwera[5]
[1]Independent Consultant, Nutritionist, Nairobi, Kenya, [2]Tampere University, Health Sciences, Tampere, Finland, [3]KEMRI-Wellcome Trust Research Programme,, Medical And Health Sciences, Kilifi, Kenya, [4]MRC Unit, The Gambia, London School Of Hygiene And Tropical Medicine,, Banjul, Gambia, [5]Liverpool School of Tropial Medicine, Paediatrics, Liverpool, United Kingdom

Background: Stunting (i.e., length for age more than 2 standard deviations below the median for the World Health Organisation (WHO) growth reference standards), is the most common form of childhood malnutrition. In 2020, 149 million children under the age of five years were stunted worldwide. These unacceptably high numbers suggest that despite global efforts to achieve Sustainable Development Goals, this is unlikely to occur without the introduction of policies and strategies to accelerate progress. The COVID-19 pandemic reversed any gains that had been made pre-pandemic by increasing food insecurity, and poverty and reducing access to maternal and child health services. In addition, the complexities of how social inequalities influence childhood stunting are elucidated to inform future strategies. Methods: Two co-authors conducted independent searches utilizing the Population, Intervention, Comparator, and Outcomes (PICO) framework. An extensive search was conducted in PubMed and Google Scholar of articles on childhood stunting in developing or low-and middle-income countries published between June 1, 2021, and June 30, 2022. We included recent data on the following themes: mechanisms, and complex pathways underpinning childhood stunting, nutrition-specific and nutrition-sensitive interventions including maternal health/well-being and women's economic empowerment, as well as insights into how to improve governance, monitoring, and evaluation of nutrition interventions at the grassroots level and providing more robust and timely impact assessments. Results: The data on "pathways and trends" showed that children with Shigella who were treated with WHO-recommended antibiotics saw a significant improvement in linear growth. A longitudinal analysis of 6 countries looking at the "consequences" of childhood stunting revealed that childhood stunting cost the private sector up to 1.2% of national GDP. A study evaluating the impact of women's empowerment from six countries in Africa and Asia reported that women's empowerment was linked to higher child height-for-age z score (Coeff 0.567, SE=0.226 p=0.002). Stunting was 12-14% (95%CI (9, 15) lower in children who took the SQ-LNS compared to those who did not, according to pooled data from 14 randomized controlled trials of small-quantity lipid-based nutrient supplements. SQ-LNS had a greater impact on female than male children, reducing the prevalence of stunting by 16% versus 9%. Finally, data on "policy and governance" revealed that the use of nutrition monitoring tool applications impacted program development by increasing the capacity of political actors and/or consumers by fostering an atmosphere where stakeholders and government partners were more confident in their ability to interpret nutrition-related evidence.

IS014 / #163

PLENARY SESSION 03: YEARBOOK
03-31-2023 14:00 - 15:15

OBESITY, METABOLIC SYNDROME AND NUTRITION

Shlomit Shalitin
Schneider Children's Medical Center of Israel, The Jesse Z. And Sara Lea Shafer Institute Of Endocrinology And Diabetes, National Center For Childhood Diabetes, GIVAT SHMUEL, Israel

The increasing number of young patients with obesity worldwide is a major challenge for health care systems in industrial and in low- and middle-income countries. Obesity is associated with an increased individual risk for the development of cardio- metabolic comorbidities, as well as by a decrease in health-related quality of life.

A sedentary lifestyle and high caloric diet combined with a genetic predisposition have been shown to be a key factor in developing obesity.

Recent data suggest that the early life environment can have lasting effects on the physiology and metabolism of the fetus and is associated with the early metabolic programming of human health. Some studies reviewed in this chapter show that a number of in-utero exposures such as maternal diet and maternal intake of non- nutritive sweeteners during pregnancy are associated with the subsequent development of childhood obesity and metabolic risk of the offspring. A metabolic signature at birth may help elucidate the mechanisms involved in metabolic health later in life. One of the reviewed studies investigate metabolic changes in cord blood that may predict subsequent infant overweight and obesity.

Early life nutrition also has a significant impact on lifelong health. One of the studies evaluated the impact of cow's milk fat consumption during infancy and childhood and child adiposity. Its findings demonstrate that compared to children who consumed reduced fat milk, children who consumed whole milk had lower odds of overweight and obesity. Another study revealed that higher fruit juice intake in infancy was associated with greater abdominal adiposity in mid-childhood and early adolescence.

School environments that support healthy food behaviors may positively influence childhood obesity. School free fruit and vegetable (FFV) policies are used to promote healthy dietary habits and tackle obesity; however, a recent reviewed study observed that the nationwide FFV policy did not have any notable beneficial effect on weight status.

Other studies included in this chapter evaluated the impact of the diet composition on adiposity, fat distribution and cardiometabolic risk markers. Childhood of different nutrient intakes were differentially associated with adolescent body fat accumulation. Additionally, the impact of higher consumption of ultra-processed foods during childhood on increased adiposity is presented. One study found that the replacement of dietary carbohydrates with fats had favorable

effects on lipoprotein cholesterol concentrations in adolescents and adults when fats were consumed as monounsaturated or polyunsaturated fatty acids but not as saturated fatty acids. In adults, the benefits of a high adherence to the Mediterranean Diet (MD) to prevent cardiovascular events are widely known. A current systematic review presented in the chapter assessed whether interaction effects occur between an obesity genetic risk score and the adherence to MD on adiposity and metabolic syndrome also in the young ages.

Children with obesity are prone to develop obesity-related comorbidities. One of the main comorbidities is non-alcoholic fatty liver disease (NAFLD). Current data found that dietary sugar restriction reduces hepatic de novo lipogenesis and fasting insulin, in addition to reductions in hepatic fat among adolescents with NAFLD.

An additional study evaluated the potential relationship between vitamin D and cardiometabolic risk among children, and reported that vitamin D supplementation had positive effects on HDL cholesterol, LDL cholesterol, and total cholesterol, with several significant changes persisting during the post-supplementation period.

Finally, considering the deleterious consequences of obesity in childhood, public health interventions are urgently called to take nutritional measures with policies that encourage healthy eating among children.

We review a selection of 15 notable articles published between July 2021 and June 2022, focusing on the relation between nutrition, obesity, and metabolic comorbidities from infancy to childhood and young adulthood.

IS015 / #165

PLENARY SESSION 03: YEARBOOK
03-31-2023 14:00 - 15:15

COGNITION

Carlo Virginio Agostoni[1], Silvia Bettocchi[2]
[1]University of Milan - Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Pediatric Area, Milan, Italy, [2]Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Pediatric Unit, Milan, Italy

Pregnancy, infancy and childhood represent the sensitive periods and many studies have been performed to understand the specific mechanisms that take place during these phases and how diet may affect them in association with other variables. It is widely documented that neurodevelopment is influenced by either genetic and environmental factors. Environmental factors, mainly represented by lifestyle, are modifiable contributors to neurovelopment. Modifiable factors include dietary patterns, whole foods (f.i. human milk) and intakes of specific nutrients from infancy to chilhood. Accordingly, even the periconceptional period and pregnancy, represent sensitive phases that should be monitored to optimize offspring's brain growth and cognitive functions. This chapter includes a selection of studies performed in the area of nutrition and cognition, published between July 1, 2021 and June 30, 2022. Original articles comprising randomized controlled trials (RCTs), observational studies, and reviewshave been selected and grouped into 4 categories, respectively: dietary patterns, micronutrients, LC-PUFA and toxicity

IS016 / #166

PLENARY SESSION 03: YEARBOOK
03-31-2023 14:00 - 15:15

NUTRITION AND GROWTH IN CHRONIC DISEASES

Anat Guz-Mark[1,2], Raanan Shamir[1,2]
[1]Schneider Children's Medical Center of Israel, Institute Of Gastroenterology, Nutrition And Liver Diseases, Petach Tikvah, Israel, [2]Tel-Aviv University, Sackler Faculty Of Medicine, Tel-Aviv, Israel

The fascinating and complex process of growth and the changes in body composition, are subjected to various alternations when facing chronic diseases during childhood and adolescence. Many chronic diseases can potentially result in growth impairment, due to numerous coexisting contributing factors that include suboptimal nutrition, high energy needs, chronic inflammation, and hormonal imbalance.

Eight leading articles were selected and reviewed in this chapter, highlighting different aspects of growth and nutrition in five major chronic diseases of childhood: asthma, celiac disease, inflammatory bowel disease, cholestatic liver disease and chronic kidney disease. We encourage the readers to explore the various topics discussed in this chapter, and to expend their knowledge in contemporary issues regarding pediatric chronic diseases and their interaction with the process of growth and nutritional status.

IS017 / #167

PLENARY SESSION 03: YEARBOOK
03-31-2023 14:00 - 15:15

PREGNANCY: IMPACT OF MATERNAL NUTRITION ON INTRAUTERINE FETAL GROWTH

Yariv Yogev, Matan Anteby, Liran Hiersch
"Lis" maternity hospital, "Sourasky" medical center, Tel Aviv University, Israel, Obstetrics And Gynecology, Tel Aviv, Israel

This chapter of the 2023 edition of the YEARBOOK on NUTRITION AND GROWTH reviews important manuscripts published between July 2021 and June 2022 addressing the association of maternal nutrition during pregnancy and intrauterine fetal growth. In the current edition, eight studies with high impact were chosen, most of which were human clinical trials. In the center of attention were studies that not only showed the associations of maternal malnutrition and abnormal fetal growth but also addressed changes reflected by the placenta. Despite the importance of human studies in this field, animal studies are not to be overlooked as they pave the way for future human studies in fields with scant medical evidence. Hopefully, this chapter will spark enthusiasm in healthcare providers and researchers to design future studies addressing this important topic.

IS018 / #23

PARALLEL SESSION 03 :NUTRITIONAL STATUS AND MICROBIOME OF THE SHORT CHILD
03-31-2023 15:45 - 17:15

ASSESSMENT OF NUTRITIONAL STATUS IN THE DIAGNOSTIC EVALUATION OF THE SHORT CHILD

Hester Vlaardingerbroek
Willem-Alexander Children's Hospital – LUMC, Pediatric endocrinology, Leiden, Netherlands

For a proper diagnostic evaluation of the short child, the clinician should: 1) remember the frequent and/or relevant causes of short stature; 2) know relevant questions/elements in medical history, physical examination and growth curve analysis; 3) perform screening (laboratory and radiology); 4) collect all diagnostic clues for primary or secondary growth disorders (intrinsic or extrinsic to the epiphyseal growth plate, respectively), assess their probability and decide on any further testing. In the past medical history, one should inquire about birth size (to estimate intrauterine growth and nutrition) and feeding problems in infancy and young childhood, which are associated with environmental enteropathy, coeliac disease, IGF1R haploinsufficiency and various syndromes (Prader-Willi, Silver-Russell syndrome, Noonan). The current medical history should include a dietary history, and thereby uncover a poorly-planned or raw vegan diet (associated with potential nutritional deficiencies) or other poor dietary practices. It also would enable an estimate of the likelihood of an iatrogenic cause of poor growth, e.g. methylphenidate treatment, psychosocial short stature or anorexia nervosa. At physical examination and growth curve analysis, the relationship between length or height SDS versus body mass index (BMI) SDS offers clues for estimating the likelihood of several diagnoses. A decreasing or low BMI SDS in a short child is suspected for environmental enteropathy, Crohn’s disease, anorexia nervosa, IGF1R haploinsufficiency, or Silver-Russell syndrome. If growth failure is combined with an increasing or high BMI, one should perform diagnostic studies for hypothyroidism, Cushing syndrome and intracranial tumours. At laboratory screening, indications can be found for several causes of poor growth, such as anaemia; deficiencies of cobalamin, iron or vitamin D; coeliac disease; hypothyroidism; or growth hormone deficiency or insensitivity (by low serum IGF-I). In adolescents with a low or decreasing BMI inflammatory markers in blood and faeces calprotectin should be screened to detect Crohn’s disease. In case of abnormal screening results or a history of ill-planned vegan diet, further specific laboratory testing is indicated.

IS019 / #24

PARALLEL SESSION 03 :NUTRITIONAL STATUS AND MICROBIOME OF THE SHORT CHILD
03-31-2023 15:45 - 17:15

PITFALLS IN DIAGNOSTIC EVALUATION OF GROWTH AND ENDOCRINE TESTS IN OVERWEIGHT CHILDREN

Erica Van Den Akker
Erasmus MC Sophia Children's Hospital, Pediatrics, Div Pediatric Endocrinology And Obesity Center Cgg, rotterdam, Netherlands

Pitfalls in Diagnostic Evaluation of Growth and Endocrine Tests in Overweight Children

Conclusion: Endocrine conditions, such as growth hormone deficiency, hypothyroidism, or hypercortisolism can lead to obesity but rarely the cause of it. Endocrine testing is recommended only in children who have short stature or decreased growth velocity in combination with weight gain. BMI specific cutoffs need to be developed.

Background. Overweight and obesity affect nearly one in three children in the WHO European Region[1]. As a result, many of the children visiting the outpatient clinics for a variety of complaints are overweight or obese. The most common cause of obesity is multifactorial, with a combination of factors, including lifestyle and genetic predisposition[2]. A single underlying medical disease as cause of the obesity is rare, but important to identify as it needs a different treatment. In children presenting with short stature or height deceleration in combination with weight gain, diagnostic tests to exclude endocrine disorders such as hypothyroidism, growth hormone deficiency or hypercortisolism should be performed[2]. However obesity leads to changes is hormonal regulation systems. Therefore the question arises on how this can influence the results of endocrine diagnostic tests. What do we use as reference range when performing hormone tests in children with overweight or obesity? Do the same reference ranges as in normal weight children apply? When are the test results abnormal? In which tests should we consider BMI specific reference ranges?

Hypothyroidism. In adults of the general population, TSH is positively correlated with BMI, while FT4 and BMI show no correlation. In children, a positive correlation is found between TSH and BMI while a negative correlation is found for FT4[3]. Because differences are small, the reference ranges for children with overweight and obesity are not different than for children with normal weight but discussion is ongoing whether there should be BMI adjusted reference ranges[4]. In extreme obesity, incidence of subclinical hypothyroidism is higher than in normal weight persons. Thyroxine treatment for obesity has no effect on weight in the absence of hypothyroidism.

Growth hormone deficiency. Peak stimulated growth hormone levels decrease with increasing BMI . However, current guidelines do not guide how to interpret the peak GH values of children

with overweight or obesity. Weight status has to be taken into consideration when performing a growth hormone stimulation test in children[5].

Hypercortisolism. If hypercortisolism is suspected, the guideline recommends to perform three screening tests: 24h-urine free cortisol, midnight cortisol; and the 1mg dexamethasone suppression test (1mg DST). Serum and salivary cortisol levels are not affected by obesity. Urine free cortisol concentration is higher in obese subjects than in normal weight subjects. but usually not higher than 3x the upper limit[6]. The sensitivity of the dexamethasone suppression test is lower in obese patients than in normal weight patients[6]. These differences in test results between normal weight and obese subject may complicate diagnosing or excluding hypercortisolism in obesity.

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IS020 / #87

PARALLEL SESSION 03 :NUTRITIONAL STATUS AND MICROBIOME OF THE SHORT CHILD
03-31-2023 15:45 - 17:15

STUDY OF GUT MICROBIOME IN CHILDREN WITH IDIOPATHIC SHORT STATURE

Liora Lazar[1], Adi Eshel[2], Leylan Moadi[3], Michal Yackobovitch - Gavan[4], Biana Shtaif[1], Meytal Bar-Maisels[1], Michal Nevo[1], Moshe Phillip[1], Sondra Turjeman[2], Omry Koren[2], Galia Gat-Yablonski[1]
[1]Schneider Children's Medical Center, Endocrinology And Diabetes, Petach Tikva, Israel, [2]Bar Ilan University, Azrieli Faculty Of Medicine, Safed, Israel, [3]Bar Ilan University, Azrieli Faculty Of Medicine, safed, Israel, [4]Schneider children's medical center, Endocrinology And Diabetes, Petach Tikva, Israel

The association between gut microbiota (GM) and linear growth in healthy middle-class young children from Western developed countries has not been thoroughly investigated. The Objectives were to investigate the relationship between GM and food consumption/eating behavior in short and lean pre-pubertal children compared to their normal height siblings.

Sixty healthy pre-pubertal children aged 3-9 years were recruited: 30 short and lean (idiopathic short stature, ISS); 30 normal height and weight siblings. Anthropometric measures, nutritional consumption, eating behavior (Child Eating Behavior Questionnaire), fecal microbial composition (16S rRNA) and metabolomics were assessed.

Despite the significant differences in anthropometric measurements, eating habits, and food enjoyment ($p<0.001$;$p<0.001$;$p=0.014$, respectively), the children with ISS consumed the same amount of nutrients as their siblings, with a balanced macronutrient distribution. GM analysis revealed a significant difference between the ISS and the siblings groups ($p<0.01$); the siblings samples were clustered together whereas the ISS samples were divided into two subpopulations, S1 similar to and S2 distinct from siblings. The phylum Euryarchaeota was found exclusively in the ISS group, whereas the genus Methanobrevibacter was significantly higher in ISS subgroup S2. The only clinical difference between the two ISS subgroups was the significantly shorter stature of children from the S2 subgroup ($P=0.022$).

Based on the presence or absence of Methanobrevibacter, two subgroups of children with ISS were identified; the cohort with more archaea was shorter in stature, implying that higher levels of archaea may be associated with slower linear growth.

IS021 / #26

PARALLEL SESSION 04: NUTRITION FOR THE PRETERM INFANT
03-31-2023 15:45 - 17:15

SHOULD WE FEED FEMALES AND MALES DIFFERENTLY TO AFFECT OUTCOMES?

Pradeep Alur
Penn State Health-Hampden Medical Center, Pediatrics-neonatology, Enola, United States of America

There are several naturally occurring sex differences beginning with pregnancy. In the early 18th century, Clarke from Royal College in London noted higher stillbirths and neonatal mortality amongst males than females. It is recognized that preterm births are more common in pregnancies with male fetuses. The OBEGEST cohort study, which examined the association between gestational diabetes (GDM) and children overweight at 5–7 years, observed that exposure to GDM is a risk factor for childhood overweight in boys but not girls. Male offspring born from pregnancies complicated by GDM had higher BMI compared with non-GDM offspring and had an increased risk of later obesity; the adjusted relative risk [RR, 95% confidence interval (CI)] was 1.47 (1.11–1.95) for all age groups. The EPICure study group showed that compared to extremely preterm female infants; males were twice at risk for severe impairment in overall cognitive scores at six years of age (OR 56 (13-250). The evidence from these and other similar reports raises the question that there may be sex differences in newborns' nutritional requirements, especially preterm infants. This current review aims to reexamine the available evidence from human milk-associated studies and discuss the possibility of sex differences in the nutritional needs of preterm infants.

The growth of male fetuses is higher than that of female fetuses throughout the pregnancy. Postnatal growth characteristics are also sex-specific; hence, the need for specific anthropometric standards for male and female preterm infants, such as Fenton's growth chart 2013, beginning at 22 weeks gestation. The intergrowth 21st project showed that boys have higher fat-free mass as early as 34 weeks of gestation ($p<0.001$). The body fat percentage (BF%) is higher in females at 10.7% vs. 9.6% in males, and this difference increases over the first few months. Hence, one should ponder if growth rates are different; should the nutritional needs be different?

Data from 12 countries using a standardized, stable isotope methodology over 14 days studied the milk intake from 2 weeks of age till 12 months. They observed that boys (n=555) consumed significantly more than girls (n=551). A recent retrospective study suggested sex-specific differences in formula consumption in late preterm infants. Naturally produced breast milk has a sex-specific nutrient composition in both animals as well as in humans. A large same-sex twin study suggests that a mother's own milk (MOM) provides sex-specific growth advantages probably related to the calibration of a mother's milk based on her newborn's sex.

Formula composition does not vary with infant sex, which may be one reason body composition data favors MOM over formula. Studies have shown sex differences in infants' macronutrient

requirements, such as preterm females may have higher fat requirements. In contrast, preterm males may have higher protein requirements for optimal growth and neurodevelopmental outcomes. Future studies must determine if we need sex-specific donor human milk (DBM) for preterm infant nutrition.

IS022 / #27

PARALLEL SESSION 04: NUTRITION FOR THE PRETERM INFANT
03-31-2023 15:45 - 17:15

MICRONUTRIENTS

Walter Mihatsch
Ulm University and Neu-Ulm University for Applied Sciences, Pediatrics And Health Management, Schwaebisch Hall, Germany

Micronutrients are vitamins and minerals needed by preterm infants in small amounts in addition to the classical macronutrients such as protein, glucose and fat. However, their impact on a health and long-term outcome are critical, and deficiency in any can cause severe and even life-threatening conditions. They perform a range of functions and are essential for growth and development, but there are risks for both deficiency and toxicity. The intake of micronutrients is sometimes not known by clinicians, but depends on the composition of enteral and parenteral nutrition products used and the nutrition regimens. Even when considering macronutrient intakes and severity of illness, several micronutrients Have been reported to be independent predictors of postnatal growth. It has been found that low intakes of folate were associated with poor weight and length growth. High iron intakes have been reported to be associated with poor length and HC growth by some authors but also with improved neurodevelopmental outcome by others. Optimized early micronutrient intakes may improve early growth in extremely preterm infants.

The aim of the present presentation was to describe recent developments in selected micronutrient needs and recommendations in preterm infants

The results of the presentation highlight the need for randomized controlled trials regarding micronutrient needs in preterm infants, using single or multiple micronutrients.

IS023 / #28

PARALLEL SESSION 04: NUTRITION FOR THE PRETERM INFANT
03-31-2023 15:45 - 17:15

MILK, GROWTH AND MORBIDITIES IN PRETERM INFANTS: A COMPLEX INTERPLAY

Magnus Domellof
Umea University Hospital, Paediatrics, Umea, Sweden

Breast milk has many health benefits in term infants, including reduced risk of infections, lower risk of obesity and improved neurodevelopment. In preterm infants, it has the additional benefit of reducing the risk of necrotizing enterocolitis. Infant formula and preterm formula aspire to achieve similar nutrient intakes and health benefits as breast milk, but this is challenging since breast milk is a highly complex biological tissue, containing complex oligosaccharides, non-protein nitrogen, nucleotides, complex lipids, growth factors, hormones, cytokines, bioactive peptides, enzymes, immunoglobulins, live leucocytes, probiotic bacteria and exosomes. There is much research interest in trying to identify bioactive components in breast milk that confer specific health benefits to preterm infants and that could be added to preterm formula or given to preterm infants as a separate supplement. Some components such as different species of probiotics, long-chain polyunsaturated fatty acids, glutamine, arginine, milk fat globule membrane, choline and oligosaccharides are currently being investigated for their effects on NEC, sepsis, neurodevelopment, etc. An alternative theory is that there are detrimental components in cow's milk, which has led to the development of human milk based human milk fortifiers. The most recent evidence for these different interventions will be discussed. Even though donor milk is recommended when the mother's own milk is not available for the preterm infant, donor milk has lower concentrations of bioactive components. In addition to breast milk banks, provision of lactation support is very important. An example of a clinical routine for extended lactation support during the first two postnatal weeks will be presented.

IS024 / #29

PLENARY SESSION 04: SLEEP, GROWTH AND OBESITY: FROM FETAL LIFE TO ADOLESCENCE
03-31-2023 17:30 - 19:00

MATERNAL SLEEP IN PREGNANCY AND OFFSPRING'S GROWTH

Riva Tauman
Tel Aviv Sourasky Medical Center, Sackler School of Medicine, Tel Aviv University, Sagol-Sieratzki Institute for Sleep Medicine, Tel Aviv, Isarel

Pregnancy is a window into the future health of both mothers and their offspring. Healthy intrauterine environment is required for normal fetal development and healthy newborn outcome. The effect of the intrauterine environment is first manifested in fetal growth then in the growth parameters at birth and echoes throughout early childhood. Infants born small or large for gestational age are at increased risk for obesity, diabetes and cardio-metabolic disease later in life. Several maternal factors such as hypertension and gestational diabetes mellitus are well known to affect the intrauterine environment and therefore treated during pregnancy. However, other factors like sleep, are less studied and not treated, yet are known to affect fetal growth and development.

Poor sleep has emerged in recent years as a contributor to adverse pregnancy outcomes, and the placenta was suggested to play a role in mediating the effect of maternal sleep on offspring growth.

Healthy sleep encompasses adequate sleep duration and timing, regularity of sleep-wake patterns and good sleep quality. Maternal sleep duration and timing have been shown to be associated with adverse pregnancy and birth outcomes. The physiologic and hormonal changes occurring during pregnancy, place women at risk for developing sleep disordered breathing (SDB). Maternal SDB appears to be an exposure that affects fetal growth and development.

Review of the current literature on maternal sleep and offspring's growth and development will be presented.

IS025 / #32

PLENARY SESSION 04: SLEEP, GROWTH AND OBESITY: FROM FETAL LIFE TO ADOLESCENCE
03-31-2023 17:30 - 19:00

CIRCADIAN SLEEP DISORDERS AND METABOLIC HEALTH IN ADOLESCENTS

Yael Weintraub[1,2]
[1]Schneider Children's Medical Center of Israel, Institute Of Gastroenterology, Nutrition And Liver Diseases, Petach Tikva, Israel, [2]Tel Aviv university, Sackler School Of Medicine, Tel Aviv, Israel

Sleep is critical for the healthy development of children and adolescents. In the teenage years sleep is related to mood and mental health, school performance, as well as physical health, weight status and growth. The processes controlling sleep regulation: sleep pressure and the circadian rhythm, change drastically during adolescence.

The circadian clock system is a homeostatic system that regulates most biological activities, such as physiology, metabolism, and behaviors. It is an evolutionarily conserved system by which organisms adapt their metabolic activities to environmental inputs. Disruption of the circadian rhythm has been linked to disintegration of metabolic homeostasis, leading to the development of metabolic complications.

Obesity and metabolic health have traditionally focused on poor diet and insufficient physical activity as major risk factors. However, there is increasing body of evidence that both sleep duration and timing, quality and regularity of sleep independently predict health trajectories and metabolic risk. Impaired sleep quality and duration have been associated with adiposity, obesity, insulin resistance and risk of diabetes and cardiovascular disease.

Psychosocial factors that may prevent good sleep and lead to abnormal sleep patterns in teenagers include social activities, behavioral factors, school schedules and technology use. Poor sleeping habits come alongside with inappropriate timing of sleep, food intake and exercise, further contributing to the development of obesity-related complications.

Lifestyle factors that disrupt the circadian clock are associated with metabolic complications. Such factors include screen time before bed-time, social jet-lag and shift working. Adolescents with a late chronotype or delayed sleep phase syndrome are even more prone to develop such long-term complications.

Acquiring healthier eating, physical activity, and sleeping behaviors affect metabolism and weight regulation by entraining the circadian rhythm.

IS026 / #5

PLENARY SESSION 05: NOVEL FOODS
04-01-2023 8:30 - 10:00

WHAT ARE THEY AND HOW TO ASSESS THEIR SAFETY?

Helle Katrine Knutsen
Norwegian Institute of Public Health, Department Of Food Safety, Oslo, Norway

In the EU, Novel Foods are foods or ingredients that have not been used for human consumption to a significant degree in the EU before 15 May 1997 (Regulation 2015/2283). The safety evaluation of all Novel Foods in the EU is performed by the European Food Safety Authority (EFSA).

EFSA evaluates the safety of NF based on dossiers provided by the applicants and according to the "Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283" (EFSA Journal 2016;14(11):4594). According to the Regulation, Novel Foods should fall under at least one of the following categories: new production process; new or modified molecular structure; from micro-organisms, fungi algae; vitamins and minerals from new process/nanomaterials; of mineral origin; from animal and their parts; cell or tissue cultures derived from animals/plants/fungi/algae; engineered nanomaterials; exclusively in food supplements. The safety assessment is based on data provided by the applicants as well as additional data requested by EFSA during the assessment in cases of missing or incomplete information. The following topics are addressed: Identity of the novel food; Production process; Compositional data; Specifications; History of use of the novel food and of its source; Proposed uses and use levels and anticipated intake; Absorption, distribution, metabolism, and excretion (ADME); Nutritional information; Toxicological information; Allergenicity. Both the ADME and the toxicological assessments follow tiered approaches. EFSA's novel food assessments address whether the novel food is safe under the proposed conditions of use and whether the normal consumption of the novel food would be nutritionally disadvantageous. Importantly, benefit(s) are not part of the assessment. All assessments of novel foods are published in the EFSA Journal after adoption. Authorisations of novel foods and placing them on the Union list are under the remit of the EU commission and the member states.

IS027 / #6

PLENARY SESSION 05: NOVEL FOODS
04-01-2023 8:30 - 10:00

DO WE NEED NOVEL FOODS IN PEDIATRIC NUTRITION?

Harry John Mcardle
University of Aberdeen, Rowett Research Institute, Aberdeen, United Kingdom

Paediatric nutrition is the maintenance of a proper, well-balanced diet, consisting of essential nutrients and adequate caloric intake, appropriate for the stage of development of the child. Changes during the immediate postnatal period are the most significant in terms of future health and well-being, so I will concentrate primarily on milk substitutes, more especially because I think this is an area where most potential exists for improvement. Many studies have shown that growth and development are less optimal in babies fed formula or substitutes than those who are given breast milk. However, it is not always possible to provide breast milk to the infant, and various formulae have been developed, and continue to be developed, to try and provide an acceptable substitute.

Originally, animal milks were used, but the first synthesised milk was invented in 1865 and by 1883 there were 27 patented infant foods. The original substitutes were primarily of animal milk with the addition of various ingredients such as wheat and malt flour and potassium bicarbonate. As time went on, various ingredients were added to improve quality of the food. A good example of this is the development of human milk fat substitutes. The first, up to about the 1920s, provided fats for energy. Between the 20s and the 90s, fatty acids were added and from then to the present, triacylglycerols and complex lipids were added. The structure of lipids in milk is also important. Fat globules consist of a triacyl glycerol core, surrounded by plasma membrane derived from the secretory cells.

Currently, human milk substitute constituents are controlled. The list of required nutrients is given in the Codex Alimentarius. Other ingredients can be added if shown scientifically to be of benefit. Importantly, human milk has many “non-nutritional” components, that perform diverse physiological functions, not all of which are completely understood. These include different cell types, bioactive components, growth factors, hormones and immunological factors. Oligosaccharides function as prebiotics and may also play a role with proteins, to act as “decoy” receptors for pathogens with affinity for the oligosaccharides on the intestinal surface. Human milk also has its own microbiome, which is very varied and which changes during lactation. The function of many of these bacteria remains obscure!

Recent studies have identified many microRNAs which may have important functions, not all of which are understood. MicroRNAs are short, noncoding RNA sequences, which act as post-transcriptional regulators of gene expression. miRNA are taken up across the infant epithelium and transferred to target tissues through the bloodstream. All of these components are important, and approaches to reproduce them and their functions could help in improving milk substitutes.

EFSA has published opinions on nutritional content of infant formula and follow-on foods. The panel concluded that nutrients and other substances should be added only in amounts that serve a nutritional or other benefit. This seems self-evident, and reduces the value of considering novel foods. However, sources of nutrients other than, for example, cow or goat milk, may become more appropriate for sustainability or economic reasons, so that continued research can be of value.

In conclusion, I have considered in some detail the composition of human milk, and how its components may play a function in normal development of the human infant. Although these may not be easy to provide, the differences between breast milk components and substitutes, and the difference in outcome between babies fed breast milk and those given substitutes, makes clear the value of continuing to find novel foods in paediatric nutrition.

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IS028 / #7

PLENARY SESSION 05: NOVEL FOODS
04-01-2023 8:30 - 10:00

NOVEL FOODS AND NEW SOURCES OF PROTEINS: THE EXAMPLE OF INSECTS

Ermolaos Ververis[1,2]
[1]European Food Safety Authority (EFSA), Nutrition & Food Innovation Unit, Parma, Italy, [2]National and Kapodistrian University of Athens (NKUA), School Of Medicine, Athens, Greece

The agri-food sector is constantly evolving, trying to meet the existing socio-economic, health-related, and environmental demands. New dietary choices are being explored, aspiring to provide additional choices to consumers. Recent advances in food science and technology enable new protein sources such as algae, cell culture-derived foods, and insects to emerge in the current food systems.

With regard to insects, certain species have been part of the diet of various populations, however, they remain a dietary novelty for most of the western population, with different regulatory frameworks globally governing the use of insects as food. In the European Union (EU) and other European countries, insects and products thereof are considered novel foods, and their safety assessment is required before potential market authorisation. The European Food Safety Authority (EFSA), the responsible EU entity for carrying out such assessments, has already concluded, with a positive outcome, the safety evaluation of several insect-derived foods and food ingredients as novel foods.

The products assessed so far derive from yellow mealworm (Tenebrio molitor larvae), lesser mealworm (Alphitobius diaperinus larvae), migratory locust (Locusta migratoria adults), and house cricket (Acheta domesticus adults), and for most of them market authorization has been already granted. These insect-derived foods comprise mainly whole insects (i.e., whole dried, whole frozen, powder); assessments of insect-derived ingredients such as protein concentrates, protein hydrolysates, and other fractions are ongoing.

Like other novel protein sources, EFSA assesses whether the consumption of insects and products thereof can be associated with health risks arising from the source per se or from the production process. Such assessments are conducted in the framework of a novel food application dossier, submitted by the food business operators who intend to market such products. Hazard identification and characterisation are performed by EFSA, by assessing the respective body of scientific evidence (requirements are described in EFSA's scientific and technical guidance documents for novel foods). Chemical and microbiological data, nutritional and toxicological information, as well as allergenicity aspects, are among the elements to be investigated. Taking into consideration also the proposed uses and use levels, an exposure assessment follows, to finally characterise any potential risk.

In the respective EFSA outputs, the high relevance of insect feed to the safety of the final products has been stressed since certain insect species can bioaccumulate hazardous compounds from the feed if present. From a nutrition point of view, it has been highlighted that the protein levels of insects can be overestimated when chitin, a component of insects' exoskeleton, is present in the final product. Furthermore, it has been emphasised that the consumption of such products can potentially induce allergic reactions in humans (sensitisation, cross-reactivity, allergens from the feed).

IS029 / #33

PARALLEL SESSION 05: NUTRITION IN THE MANAGEMENT OF PEDIATRIC INFLAMMATORY BOWEL DISEASE
04-01-2023 10:30 - 12:00

RATIONALE FOR NUTRITIONAL TREATMENT IN THE PATHOGENESIS OF INFLAMMATORY BOWEL DISEASE

Johan Van Limbergen
Amsterdam University Medical Centers - Emma Children's Hospital, Paediatric Gastroenterology & Nutrition, Amsterdam, Netherlands

Nutritional therapy with the Crohn's Disease Exclusion Diet + Partial Enteral Nutrition [CDED+PEN] or Exclusive Enteral Nutrition [EEN] induces remission and reduces inflammation in mild-to-moderate paediatric and adult Crohn's disease [CD]. Nutritional therapy addresses several key factors in the pathogenesis of Crohn's disease, is associated with mucosal healing and improves disease-associated malnutrition and quality-of-life.

Successful dietary therapy decreases the relative abundance of Proteobacteria and increases Firmicutes towards healthy controls. By Week 12, genera from Proteobacteria reached relative abundance levels of healthy controls with the exception of E. coli. We have recently shown that a decrease in kynurenine and succinate synthesis and an increase in N-α-acetyl-arginine characterized remission through CDED+PEN. In patients not achieving remission, Proteobacteria and fecal metabolites were comparable to baseline samples. Reduction in components of the kynurenine pathway, such as kynurenine and quinolinic acid, were strongly associated with remission with both CDED+PEN and EEN, which were maintained in children sustaining remission till week 12. Specific serotonin pathway metabolites, such as melatonin, N-acetylserotonin, and 5-OH-tryptophan, were significantly increased in fecal samples from patients maintaining remission at W12 with both CDED+PEN and EEN. The ratios of kynurenine and melatonin and quinolinic acid and melatonin perform well as markers for sustained remission.

Successful dietary therapy induces correction of compositional and functional dysbiosis. However, 12 weeks of diet was not enough to achieve complete correction of dysbiosis. We have shown that composition and metabolic capacity of the microbiome type are important and change quickly during the early clinical response to dietary intervention. Correction of dysbiosis may therefore be an important future treatment goal for CD.

IS030 / #34

PARALLEL SESSION 05: NUTRITION IN THE MANAGEMENT OF PEDIATRIC INFLAMMATORY BOWEL DISEASE
04-01-2023 10:30 - 12:00

EXCLUSIVE ENTERAL NUTRITION FOR THE TREATMENT OF PEDIATRIC CROHN'S DISEASE

Raanan Shamir
Schneider's Children Medical Center of Israel, The Institute of Gastroenterology, Nutrition and Liver Diseases, Petach Tikva, Israel

Inflammatory bowel diseases (IBD), namely Crohn’s disease and ulcerative colitis are common in the pediatric population and are associated with substantial morbidity. Disease activity is associated with growth failure, mainly in Crohn’s disease where the prevalence of growth failure reaches about 40%.

Exclusive enteral nutrition (EEN) for 8-12 weeks has been shown to induce remission in the majority of patients with Crohn’s disease and in recent years the non-inferiority, and to some extent, the superiority of this modality of treatment was demonstrated compared to steroids, turning EEN into the recommended treatment of choice in many societal guidelines.

In the last decades, biologics were introduced as an efficacious treatment for IBD. Thus, the role of EEN in remission induction has to be compared to biologics. The evidence in the literature is scarce, however, there is evidence for the efficacy of EEN also when compared to biologics and also evidence for the positive effect of concomitant treatment with partial enteral nutrition and biologics, mainly in adults.

The presentation will provide an up-to-date review of the evidence, paving the way to the presentation on the emerging role of dietary regimens in the treatment of IBD.

IS031 / #35

PARALLEL SESSION 05: NUTRITION IN THE MANAGEMENT OF PEDIATRIC INFLAMMATORY BOWEL DISEASE
04-01-2023 10:30 - 12:00

NEW DIETETIC STRATEGIES FOR THE MANAGEMENT OF PEDIATRIC CROHN'S DISEASE: DO WE HAVE ENOUGH EVIDENCES?

Konstantinos Gerasimidis
University of Glasgow, Human Nutrition, Glasgow, United Kingdom

Nutritional epidemiology and research in animals highlight the critical role of diet in development of Crohn's disease (CD) and initiation of gut inflammation, respectively. In active and pre-surgical CD, exclusive enteral nutrition (EEN) is a highly effective therapy, but it is a treatment that is difficult to adhere to and is therefore unsuitable for long-term disease maintenance. Hence, over the past 3 decades there has been several attempts to develop new dietary therapies to induce and prolong disease remission. There are more than 20 dietary therapies reported in the peer-reviewed literature for the management of CD. Some of these dietary therapies aimed to exclude food believed to cause inflammation within animal experiments, such as food additives, processed food and read meat, others aimed to introduce a diet which align to the principles of the Mediterranean diet, increase fibre and very few studies aimed to correct microbial dysbiosis, typical of CD. CDTREAT is a solid-food based diet which aims to mimic the composition of EEN and its effects on the gut microbiome. Most of the studies which explored the effectiveness of these novel dietary therapies for CD, explored their efficacy on six different efficacy outcomes, including clinical disease activity, quality of life, gastrointestinal symptoms, blood inflammatory markers, faecal calprotectin (FC) and endoscopic/imaging scores. Very few studies explored the effectiveness of these dietary therapies on objective biomarkers of gut inflammation. It is noteworthy that the efficacy of a significant number of diets has only been described in a single publication. Most diets reported improvements in disease activity scores; nonetheless, the efficacy signal is less encouraging for the effect of these diets on objective disease activity biomarkers. The CD exclusion diet coupled (CDED+PEN) with 50% partial enteral nutrition plus 5 daily mandatory foods is the most popular diet with replication by independent groups within RCT. The specific carbohydrate diet and Mediterranean diet failed to improve inflammatory biomarkers in an RCT in adults with Crohn's disease. CD-TREAT demonstrated efficacy in a very small number of children with CD, but results from larger studies are imminent. While there is promise in this area, the current available evidence does not allow us to draw firm conclusions and recommendations regarding the efficacy of food-based dietary therapies on the management of CD; perhaps with the notable exception of CD exclusion diet with 50%PEN and the daily consumption of mandatory food. Limitations of current dietary research include the bias of placebo effect, particularly when authors report improvement in disease activity scores in patients with mild active disease. Compliance to dietary interventions is also poorly or inadequately described; mostly with self-reported dietary intake which is inherent to recall and misreporting bias. In this emerging area of clinical research and considering the inherent limitations of dietary research and assessment of disease activity objectively in IBD, replication of study results is of utmost importance before

drawing conclusions on efficacy of any dietary treatment. Exclusive enteral nutrition remains a very effective induction treatment but with the advent of biological therapies fewer patients are expected to be treated with EEN, and in the future it is likely we will see a higher use of EEN in combination with other induction therapies and for presurgical use.

IS032 / #36

PARALLEL SESSION 06: MATERNAL STRESS, LACTATION AND EFFECTS ON THE INFANT
04-01-2023 10:30 - 12:00

MOTHER-INFANT CONFLICT AND "SIGNALLING" VIA BREAST MILK

Nurul Husna Mohd Shukri[1], Mary Fewtrell[2], Jonathan Wells[2]
[1]Universiti Putra Malaysia, Department Of Nutrition, Serdang, Malaysia, [2]University College London, Childhood Nutrition Research Center, Ucl Great Ormond Street Institute Of Child Health, London, United Kingdom

Lactation is a dynamic process in which the mother and the infant actively compete over how much of the mother's resources will be invested in breast milk during lactation. The infant's demand for milk can be expressed through behaviour, appetite, vocalisation, and/or non-nutritive suckling, while the mother's response can be shown in nursing behaviour, milk production, and/or milk composition. It is hypothesised that these relationships may shape infant behaviour and feeding, particularly appetite regulation, and may thus influence infant growth and development. However, there are many unanswered questions about this tug-of-war, including who is more in charge, how the mother allocates her energy economically to maximise her offspring's fitness, and whether, for instance, an abundance of maternal energy will result in a lessening of tension. It is also acknowledged that maternal emotion could influence breast milk synthesis and ejection, highlighting the need for minimising maternal stress or promoting relaxation during the postpartum period. Furthermore, the mother's energy reserves might be considerably depleted during the early postnatal period as she recovers from birth while continuing to invest in her infant, primarily through breast milk. Because breastfeeding requires high energy, postpartum distress may intensify the tug-of-war by affecting the mother's energy budget. Aiming to reduce this mother-infant conflict, we conducted a randomised controlled trial by manipulating the maternal psychological state using relaxation therapy (breastfeeding meditation) to see the effect on maternal stress, breast milk production, and infant behaviour and growth. The trial was conducted in Malaysia among first-time mothers and their full-term infants (n = 64), who were followed up on from birth to 16 weeks in three home visit sessions. Maternal stress and infant behaviour were assessed, infant growth was monitored, and breast milk samples were collected at all visit sessions. This trial found significant relaxation therapy intervention benefits for both mothers and infants, with the strongest evidence on maternal stress reduction and achieving optimal infant weight and BMI. The intervention therapy also showed a significant effect on infant behaviour, with longer infant sleeping duration, and on milk composition, with a greater decrease in milk cortisol concentrations at the early home visit. The pooled results from early to later home visits also revealed that the intervention might have long-term or cumulative consequences on elevating total energy levels in breast milk. Overall, listening to the relaxation treatment lowered maternal stress and modified the breast milk composition, which had an influence on infant sleeping behaviour and growth. The benefits of relaxation treatment on infant outcomes might be mediated by physiological signalling via changes in breast milk composition, or behavioural signalling via the influence on sleeping duration. In conclusion, encouraging relaxation during breastfeeding shifted the mother-infant tug-of-war toward a positive energy

balance (reduced mother-infant conflict), leading to a greater energy investment in milk production and promoting healthy newborn growth. Nevertheless, it is important to consider the study's main limitations, which include the small sample size and non-blinded intervention due to the nature of behavioural intervention.

IS033 / #37

PARALLEL SESSION 06: MATERNAL STRESS, LACTATION AND EFFECTS ON THE INFANT
04-01-2023 10:30 - 12:00

MATERNAL INFLAMMATION AND MILK COMPOSITION

Ellen W Demerath[1,2], Kelsey E Johnson[3], Tim Heisel[4], Annalee Furst[5], Lars Bode[5], Cheryl Gale[6], Frank Albert[3], David A Fields[7], Ran Blekhman[8]
[1]University of Minnesota, Epidemiology And Community Health, Minneapolis, United States of America, [2]University of Minnesota School of Public Health, Epidemiology And Community Health, Minneapolis, United States of America, [3]University of Minnesota, Genetics, Cell Biology, And Development, Minneapolis, United States of America, [4]University of Minnesota, University Of Minnesota Genomics Center, Minneapolis, United States of America, [5]University of California San Diego, Pediatrics, San Diego, United States of America, [6]University of Minnesota, Pediatrics, Minneapolis, United States of America, [7]University of Oklahoma Health Sciences Center, Harold Hamm Diabetes Center, Oklahoma City, United States of America, [8]University of Chicago, Division Of Biological Sciences, Chicago, United States of America

Systemic inflammation plays an important role in the etiology of most chronic diseases but its role in shaping breast milk composition and the developing infant gut microbiome have only recently been investigated. The MILk Study is an observational cohort of 500 healthy mother-infant dyads followed from pregnancy to 6 months postpartum. Its primary goal is to assess the role of maternal obesity, diabetes, diet, and genetic factors in shaping variation in human milk, and whether differences in milk alter infant growth and health. Recent multi-omic analyses in a subset of 242 of the dyads utilized genomic material from mammary epithelial cells and other cell types found in human milk to provide insight into individual variation in mammary gene expression signatures. Our data show that 1) milk interleukin-6 (IL-6) concentration, a biomarker of inflammation, explained the most variation in milk gene expression, being correlated with expression levels of over 2000 genes, most of which fell into “inflammatory response” and related pro-inflammatory gene pathways; 2) that women with gestational diabetes had higher milk concentrations of both CRP and sialylated human milk oligosaccharides (HMOs), the latter of which were correlated with gene expression levels in multiple inflammatory pathways, and 3) that expression of JAK/STAT pathway genes in milk, particularly STAT1, was inversely correlated with the abundance and growth of infant fecal Bifidobacterium infantis abundance, a dominant microbe in the gut of breastfed infants that is known to beneficially shape the biochemical and immunological environment of the intestinal epithelium. Thus, our results suggest that mammary inflammation, as indexed by elevated IL-6 levels in the milk and evidenced by activation of pro-inflammatory gene pathways, may be an important driver of variation in milk composition, with potential effects on the infant gut microbiome.

IS034 / #38

PARALLEL SESSION 06: MATERNAL STRESS, LACTATION AND EFFECTS ON THE INFANT
04-01-2023 10:30 - 12:00

MATERNAL CAPITAL, STRESS AND INFANT GROWTH

Sarah Dib, Mary Fewtrell, Jonathan Wells
UCL Great Ormond Street Institute of Child Health, Population, Policy And Practice, London, United Kingdom

Maternal capital is a broad term referring to any aspect of maternal phenotype, including somatic, cognitive, psychological and social traits, that represent the resources that are available for maternal investment in the offspring. During pregnancy, maternal capital is the only direct source of signals that a fetus is exposed to, while during lactation the infant is exposed directly to other environmental signals, but maternal capital remains the main environment that the infant is exposed to and responds to. Previous research has shown that maternal capital was associated with infant growth, nutritional status, adult size, and even educational attainment. Therefore, strategies that enhance maternal capital could potentially improve children's health and development by improving maternal investment in the offspring during critical windows of growth. One such strategy is reducing maternal stress. We previously showed in a randomized controlled trial that reducing maternal stress by asking breastfeeding mothers of late preterm and early term infants to listen to a relaxation therapy, resulted in higher infant weight gain. The intervention also promoted maternal capital by improving verbal memory scores of mothers in the intervention group. Additionally, there were significant interactions between the intervention group assignment and maternal capital which indicated that the intervention had greater effects on infant weight, length, crying, and maternal responsiveness to infant cues among mothers with lower maternal capital. The findings suggested that a relaxation intervention could buffer against maternal capital insults, as the effects of low maternal capital appeared most detrimental to infants whose mothers did not receive the intervention. Overall, understanding and applying evolutionary concepts such as maternal capital to health-related studies could improve understanding of how the environment interacts with the mother, milk and infant. It could also help to better predict the outcome of interventional studies and achieve the desired results such as improved infant growth and promotion of breastfeeding.

IS035 / #41

PLENARY SESSION 06: MICROBIOME IN EARLY LIFE
04-01-2023 14:00 - 15:30

MICROBIOME ASSESSMENT AND ASSOCIATED CLINICAL OUTCOMES IN PRETERMS

Tim De Meij[1,2], Hendrik Niemarkt[3], Anton Van Kaam[2], Mirjam Maria Van Weissenbruch[4], Daniel Vijlbrief[5], Willem De Boode[6], Chris Hulzebos[7], Nanne De Boer[2], Boris Kramer[8], Richard Van Lingen[9], Marc Benninga[1], Veerle Cossey[10]
[1]Amsterdam UMC, Emma Children's Hospital, Amsterdam, Netherlands, [2]Amsterdam UMC, Emma Children's Hosptital, Amsterdam, Netherlands, [3]Maxima Medical Centrum, Neonatology, Veldhoven, Netherlands, [4]Vrije University Amsterdam, Pediatrics-neonatology, Amsterdam, Netherlands, [5]Wilhelmina Kinderziekenhuis, Neonatology, Utrecht, Netherlands, [6]Radboud UMC, Neonatology, Nijmegen, Netherlands, [7]UMCG, Neonatology, Groningen, Netherlands, [8]MUMC, Neonatology, Maastricht, Netherlands, [9]Isala klinieken, Neonatology, Zwolle, Netherlands, [10]UZ Leuven, Neonatology, Leuven, Belgium

Microbiome Assessment and Associated Clinical Outcomes in Preterms

Neonatal gut microbiota colonization plays an important role in promoting health on the short and long term. Early microbial functions include priming of the immune system and growth regulation. Long-term consequences of a disturbed colonization include an increased risk for allergy, asthma, and inflammatory and auto-immune diseases, and impaired neurocognitive outcome. Preterm infants, who by definition suffer from incomplete gut tissue and immune system maturation, are at increased risk for an aberrant microbial colonization by many factors, including prolonged exposure to antibiotics. Dysbiosis is considered a key risk factor for necrotizing enterocolitis (NEC) and late-onset sepsis (LOS) in this population. Since the major prognostic factors for NEC and LOS include early diagnosis and treatment, an urgent but yet unmet need exists for early, preferably preclinical and noninvasive, diagnostic biomarkers. Microbial and metabolic alterations are expected to occur before NEC and LOS onset, and could therefore hypothetically serve as a target for biomarker development and for early therapeutic, and possibly even preventive, strategies. This would provide clinicians with a window of opportunity to initiate therapy before clinical symptoms appear, probably reducing mortality rates.

In this presentation, data from an ongoing nationwide cohort study will be presented, including infants < 30 weeks of gestational age, with the aim to predict NEC and LOS onset in preclinical stage, using fecal biomarkers. For this study, over 25.000 fecal samples from 3000 infants in 9 neonatal intensive care units in the Netehrlands and Belgium, have been collected and analyzed by LC-MS, electronic-nose-technology and molecular techniques to describe microbiota composition. Furthermore, an overview is given on observed associations between gut microbiota colonization in preterm infants and short and long term health outcomes, including beneficial and negative factors influencing outcome. Novel techniques to describe the microbiome and microbial functions will be discussed.

IS036 / #42

PLENARY SESSION 06: MICROBIOME IN EARLY LIFE
04-01-2023 14:00 - 15:30

HOW DOES PRETERM MICROBIOME EXERT SHORT AND LONG TERM HEALTH EFFECTS

Janet Berrington
Newcastle University, Translational And Clinical Research Institute, Newcastle, United Kingdom

The health of preterm infants is associated with the structure and function of the gut microbiome. Studies have observed a change in gut microbiome (dysbiosis) in preterm infants who develop necrotising enterocolitis (NEC) or late onset sepsis (LOS) in comparison to preterm infants who do not. Key taxa have been identified as associated with ill health (klebsiella, proteobacteria) or good health (bifidobacteria, lactobacilli) defned as lack of these key neonatal diseases. Most data is from observational studies, where only association can be shown, but probiotic studies with mechanistic work offer insights into how these effects may be modulated, as does data from mechanistic work embedded in other enteral intervention studies in preterm infants.

In term infants breast fed infants have a different microbiome than formula fed infants. In preterm infants many factors impact the microbiome including type and amount of mothers own milk (MOM) received, antibiotics received, probiotic exposure, day of postnatal life and the neonatal intensive care unit in which the infant is cared for.

The microbiome may exert beneficial health effects via multiple mechanisms, many of which are very poorly understood especially in the preterm infant. These include competetive exclusion of pathogenic bacteria, production of metabolites that impact host physiology (such as vitamins or short chain fatty acids) or metabolites that act as substrate for other gut bacteria (bifidogenic effects). Certain taxa exhibit direct effect on gut enterocytes and tight junctions, and impact on enterocyte transcriptome. These mechanisms are impacted by host responses at both the intestinal luminal level and within the systemic circulation. Additionally some impacts are co-dependent on other factors contained in breast milk, such as human milk oligosaccharides that support the growth of specific species such as bifidobacterium. Adverse short term health effects include the dysbiosis that precedes NEC or LOS, as well as prolongation to time taken to establish full feeds and impacting on length of stay. Manipulation of the preterm microbiome with deliberately administered probiotics is possible, and an impact has been shown on both functional taxonomy and metabolic function of the microbiome.

Longer term health impacts are potentially driven by metabolic programming of the infant impacting on the likelihood of developing metabolic syndrome in later life. Other diseases have been shown in adulthood to be associated with changes in the microbiome, such as Parkinsons disease, but direct links to the preterm microbiome are currently lacking.